THE CANCER PROBLEM

A STATISTICAL STUDY

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A STATISTICAL STUDY

BY

C. E. GREEN, F.R.S.E.

SECOND EDITION

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APOLOGIA

CITAVERIT vero aliquis notum illud "ne sutor ultra crepidam," scilicet prohibens indoctum medicinæ artem medicam tractare ; tamen hunc reputare decet concedendum aliquid viro qui certum aliquod studium tanquam vitæ suæ metam amplexus postea autem impeditus ne vitæ cursum propositum sequeretur, propositum munus tantum *ἐν καίρῳ παρέργου* exercere fato cogitur.

CHAPTER I

THE CRUX OF THE QUESTION

Some years ago, after reading one of Dr. Conan Doyle's "Sherlock Holmes" stories, it occurred to me that if some of the world's great problems were attacked in a similar fashion by the deductive method some good might result.

As a former student of medicine the cancer problem at once occurred to my mind and in the course of six months I was in the grip of an enthralling if somewhat gruesome hobby.

Naturally, one first of all turned to the literature of the subject and to the latest teaching of pathology on the growth of neoplasms in all their varieties, clinical characters and microscopic appearances. Histology seems to have said its last word on the subject, but it has thrown very little light upon the problem and has done nothing to clear up the etiology of malignant disease, however valuable its processes are for purposes of diagnosis.

A study of hospital statistics followed, but beyond proving repeatedly that certain parts of the body are particularly liable to malignant disease these were practically barren of results. The statistics of the Registrar-General, however, seemed to me to be in a different category, as they clearly prove (1) that cancer is much more prevalent in some districts than in others; (2) that it is common in some trades and uncommon in others; and (3) that these figures are fairly constant.

These three facts are surely of great significance. Why should the cancer death-rate be greatly higher in the case of chimney-sweeps than in the case of grocers? Why should coal-heavers be more liable to malignant disease than coal-miners, lawyers than physicians, sailors than fishermen, furriers than tanners, lead-workers than copper-workers?

The local distribution of cancer is equally surprising.

[illegible]

In Scotland we get some very striking results. To take the two extremes, in Nairn, a beautiful rural county whose people are mainly employed in pastoral pursuits, we find a cancer mortality of 9·73 per cent., while the City of Glasgow has only 2·98 per cent.

Viewed broadly, these curious facts raise at once a sharp issue on the present theories of cancer origin: the Cell Theory, and the Parasitic.

The question at issue between these is whether cancer arises through a modification of the formative process, or is the result of stimulation by micro-organisms. In other words, is it of intrinsic or extrinsic origin? Now, if cancer be due to modifications of the formative cell processes, why should these modifications occur more frequently in some trades than in others? To say that sweeps or furriers start life as a class with their cells particularly prone to these modifications is obviously absurd.

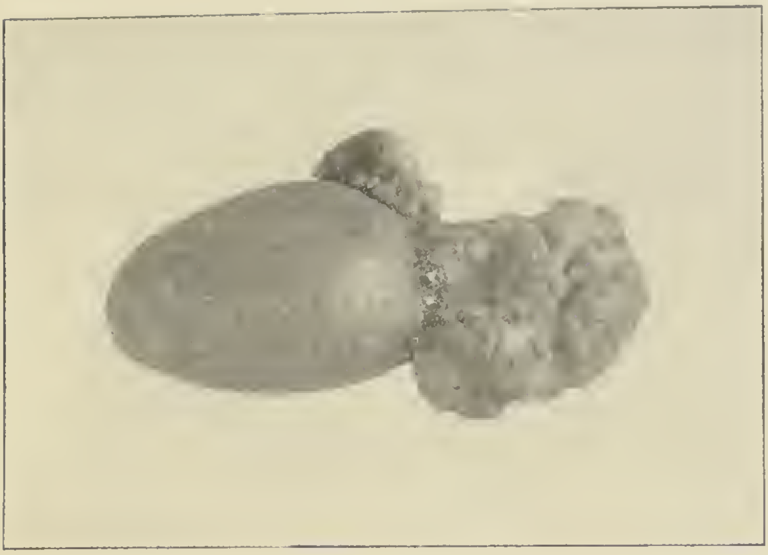
These statistics prove that *it must be some element in the environment of the sufferer which brings on the disease*, and if we admit this, we must admit an extrinsic origin.

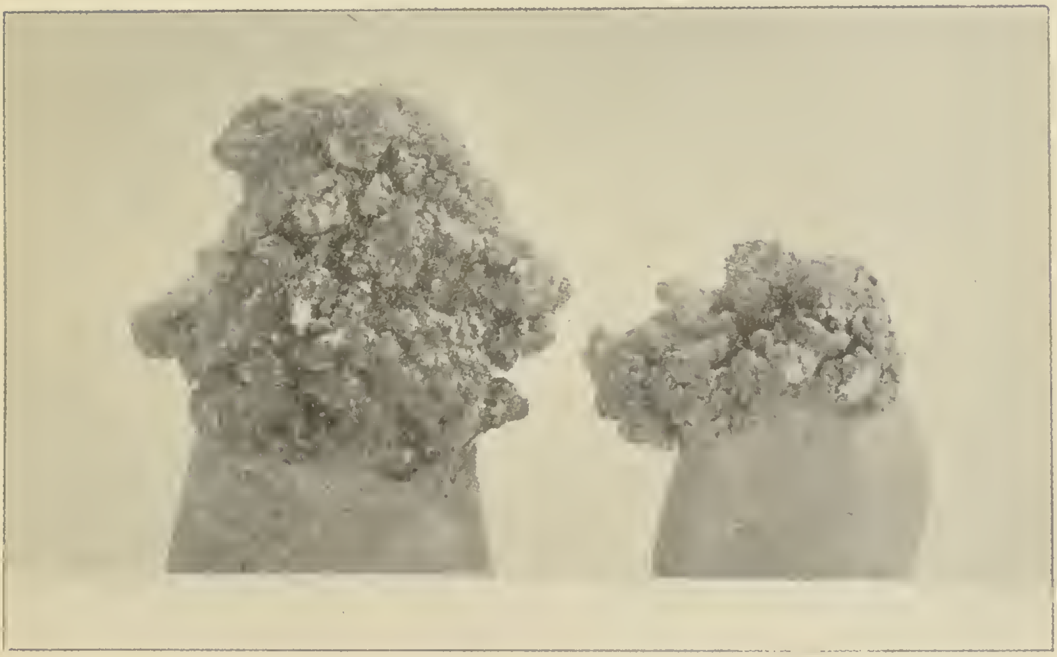
If this be so, how does it set up this strange condition of perpetual cell-growth which, pathologically, is a thing *per se*, and so far unaccountable? The extrinsic cause must be either mechanical, chemical, parasitic, or a subtle combination of the three.

Mechanical irritation is a commonly accepted factor in the etiology, but it is not a satisfactory one. It may have, like trauma generally, a predisposing effect, but it is far from being invariably present, and it is difficult to understand what mechanical irritation can cause a sarcoma of the pituitary body or even a uterine carcinoma. The longer one considers this problem the stronger the presumption becomes that the cause is biochemical or parasitic. A purely chemical action, however, will hardly account for such phenomena of cancer as metastases, if the application of the chemical be local as in petroleum cancer.

The parasitic theory of origin is at present out of fashion, but after disbelieving it and reading much that has been said against it, it seems to be the only one which will account for the high degree of proliferative activity which is the essential characteristic of the cells of malignant tumours, and the cause of all their special qualities. It is unquestionable that in the vegetable kingdom a similar condition is induced by the little-known organisms called by some biologists mycetozoa and by others myxomycetes.

One instance may be shortly referred to, simply to show how the presence of an organism of this kind strangely stimulates the cells of tubers in a manner which exactly simulates cancer. A curious disease of potatoes known as warty disease has only within





Figs. I. and II.—Warty Disease in Potatoes, due to a minute Fungoid Organism.

the last few years made its appearance in England. At the time of writing very few cases have occurred in Scotland. (See Figs. I. and II.)

Sometimes the tuber is attacked at one side or at the end only, when excrescences are formed at the side or end of the potato. These excrescences may be larger than the original tuber itself. Frequently the tuber is severely attacked when quite young; when this happens its growth is almost entirely stopped, and the whole potato is turned into a wrinkled, misshapen mass, which soon decays or dries up.

In such plant diseases, and there are many, we have instances of the stimulation of protoplasm by other protoplasm in direct contact with it. Even this, however, is not necessary.

Irritation and hypertrophy of cells may be caused, as Ward has shown, by parasites which never bring their protoplasm into direct contact with that of their host, and may stimulate it through *both cell-walls* to abnormal growth.

[illegible] that [illegible]

Not only are the cells stimulated to grow larger and divide oftener than normally, but the chlorophyll disappears, the cell-sap changes colour to red, the numerous compound crystals normally found in the tissues diminish in number and are different in shape, large quantities of starch are stored up, and even the vascular bundles are altered in character. All these changes indicate very profound alterations in the physiological working of the protoplasm of the cells of the host, and yet the fungoid germ has done its work through both its own cell-walls and those of the host. ″

If then the presence of such organisms can set up so abnormal a growth in the case of vegetable cells, is it too much to account for the unlimited cell formation which is so puzzling in the case of cancer ?

It may be said, however, that there is a wide difference between the vegetable cell and the animal, and that a class of organism which causes the former to behave in this way may not similarly affect the animal cell. This may be true, but the fact remains that many of the fungoid pests of plants are communicable to, and cause the death of, insects, and that actinomycosis in animals, for example, is undoubtedly due to the action of a fungoid germ. It must also be borne in mind that organisms such as those referred to are on the border line between plants and animals, and that their metabolism is as yet almost unknown.

One cannot enter here into a discussion of the protean forms which the minute fungi assume, or their morphology in different hosts. This remarkable phenomenon of heterœcism is one of the strangest in nature. For example, the *Peridermium pini*, which causes the growth of large blisters on the pine after the mycelium has been for years beneath the bark, has been found to be the same organism as *Coleo-spermium senecionis*, which is developed in and has practically no effect upon the leaves of the common groundsel.

Why some minute fungi should have a malignant effect upon certain hosts seems as unaccountable as why some of the larger fungi should be poisonous.

In spite of the arguments of many pathologists one feels driven to these conclusions:—

(1) The occupational and local incidence point to an infection.

(2) This infection differs from any ordinary microbic one, in respect that—

  (*a*) It does not destroy the part, but stimulates it to enormous overgrowth.

  (*b*) It has no local inflammatory reaction and practically no fever.

(3) It has, on the other hand, a strong resemblance to animal diseases caused by fungoid organisms, such as actinomycosis, which in cattle is often mistaken for cancer and scirrhus.

(4) Stimulation to enormous overgrowth in plants is, so far as known, invariably due to the presence of fungoid organisms, which it must be remembered are totally different from bacteria.

(5) Cancerous tumours of mice, originating sporadically, have been subjected for twenty minutes to the extremely low temperature of −195° in liquid air, and yet inoculations of these produced new tumours. No animal cell could then retain its vitality, but the spores of fungoid organisms could.

The analogy from these points seems too strong to be lightly set aside. I would go further and say that a study of the life-history of certain organisms, which are on the border line between plants and animals, clears up much that seems obscure in the cancer problem.

The chief objections to the parasitic theory of cancer origin are these: that so few actual parasites have been found; that the cancer cell seems itself to be the parasite; and that the heterotype mitosis, which is apparently characteristic of reproductive and germ cells, is also a feature in the multiplication of the cells of malignant tumours. To my mind all of these objections have been met by the following instance:—The saprolegniæ, one of the groups of fungi which live on dead animal matter, are themselves attacked by a mycetozoan parasite known as *Rozella*, the swarm spores of which bore their way into the growing tubes of the host. When a spore has effected an entrance in this way it remains visible for a short time in the protoplasm of the tube, and then can no longer be distinguished. It loses its individuality and is lost in the protoplasm of the tube, which at once swells out and divides by transverse walls formed in the same way as in the delimitation of sporangia in normal saprolegniæ. On these surprising effects De Bary (*Comparative Morphology and Biology of the Fungi, Mycetozoa, and Bacteria*, p. 395) makes the following comment:—

"If no later investigations bring to light facts at variance with those here given, and this, according to Fischer's statements, is not probable, but cannot, however, be considered to be impossible, the above case is an instance of *a parasite surrendering its individuality, so far as that can be recognised morphologically*, after its entrance into the host; it becomes changed into a part of its host and *the two can no longer be distinguished from one another by our present means of investigation. The parasite* *also communicates new properties to the host,* which is some two hundred times its size, and through them *the host develops into its own parasite.* This transmutation of the host by the parasitic spore which has coalesced with it, though peculiar, is yet *analogous with the fertilising effect of the spermatozoid on the oösphere* of organisms which in the sexual sense are highly differentiated from one another."

The italics are mine, but I think that no one familiar with the cytology of cancer who carefully weighs the italicised words can fail to be impressed by their importance. Here we have a parasite so behaving towards its host that its protoplasm is lost in that of its host, and that the cells of the host become its own parasite. Could anything more closely resemble the qualities of the cancer cell?

It must also be borne in mind that this parasite *Rozella* is closely akin to *Plasmodiophora brassicæ,* which causes tumours in plants, and to another known as *Woronina,* the morphology and course of development of which are so strange that De Bary himself hesitates whether to class them among the myxomycetes as plants or among the protozoa as animals.

In the case of *Plasmodiophora brassicæ* we get a remarkable example of plant malignancy. The amœboid protoplasm of the parasite lives in the protoplasm of the cells of the cruciferæ, to which it gains access through the root-hairs. It does not kill the cells, but stimulates their protoplasm to increased activity of growth and division. The externally visible result is the formation of distorted swellings on the root (popularly known as finger-and-toe, club-root or anbury).

The extent to which this organism stimulates the growth of the root-cells is shown by Figs. III. and IV. from a tumour on a cabbage root.

The organism was discovered by Woronin in 1876 and described by him in 1878. Strange to say, even at that date he predicted that malignant growths in man might eventually prove to be due to a parasite of a similar nature. This hypothesis has been advocated from time to time, but Ford Robertson and Wade (*Lancet*, January 28, 1905) have gone far towards proving it by demonstrating the presence in carcinomatous tumours of bodies corresponding in form, and in reaction to a special method, to fourteen phases in the strange life-cycle of *Plasmodiophora brassicæ*, and in growing from such tumours an organism accurately representing several

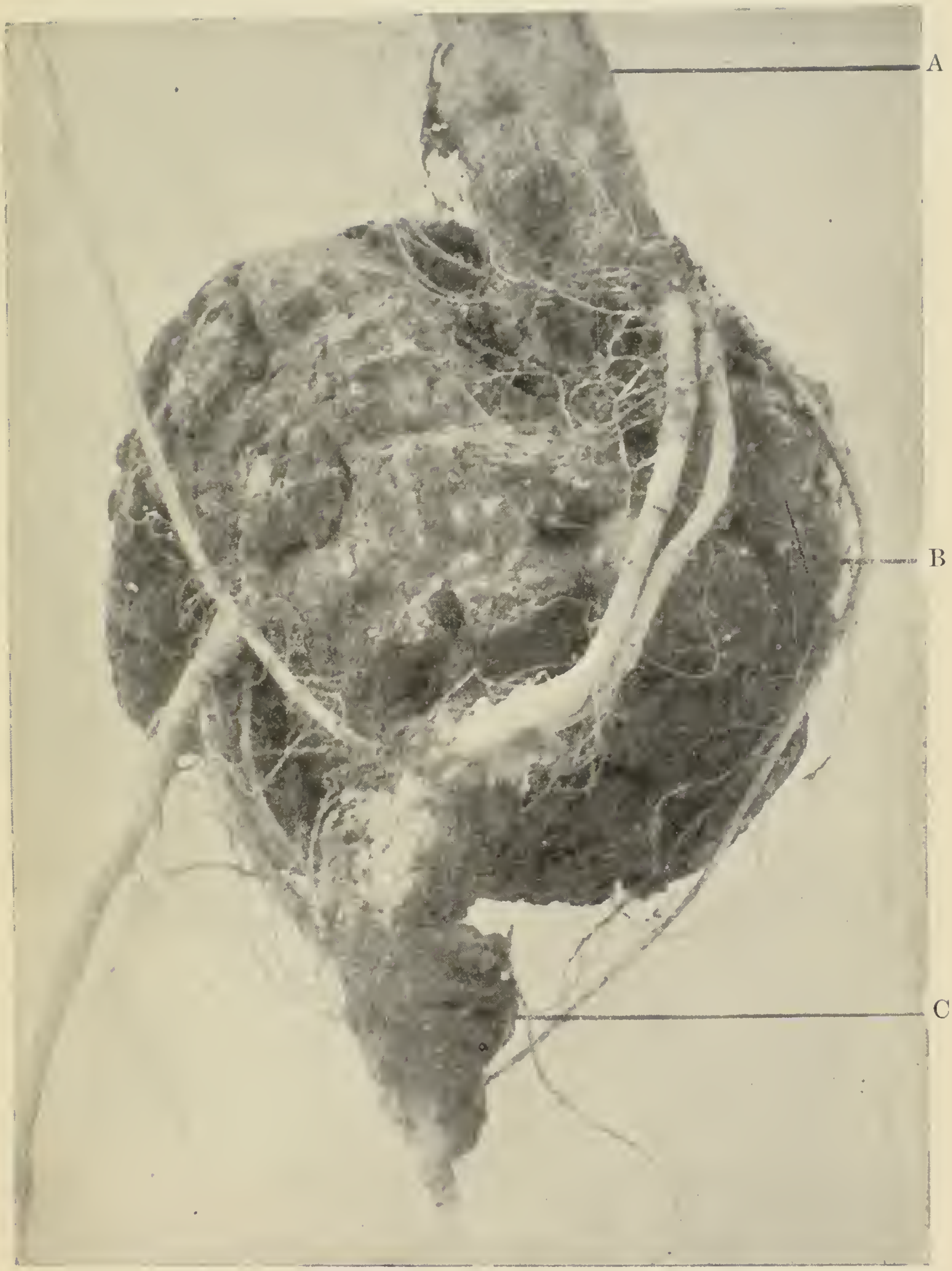


Fig. III.—Finger-and-Toe ; large Tumour on the Root of a Cabbage Plant caused by *Plasmodiophora brassicæ*. A, Stem of Plant ; B, Tumour, natural size ; C, Smaller Growth on Rootlet.

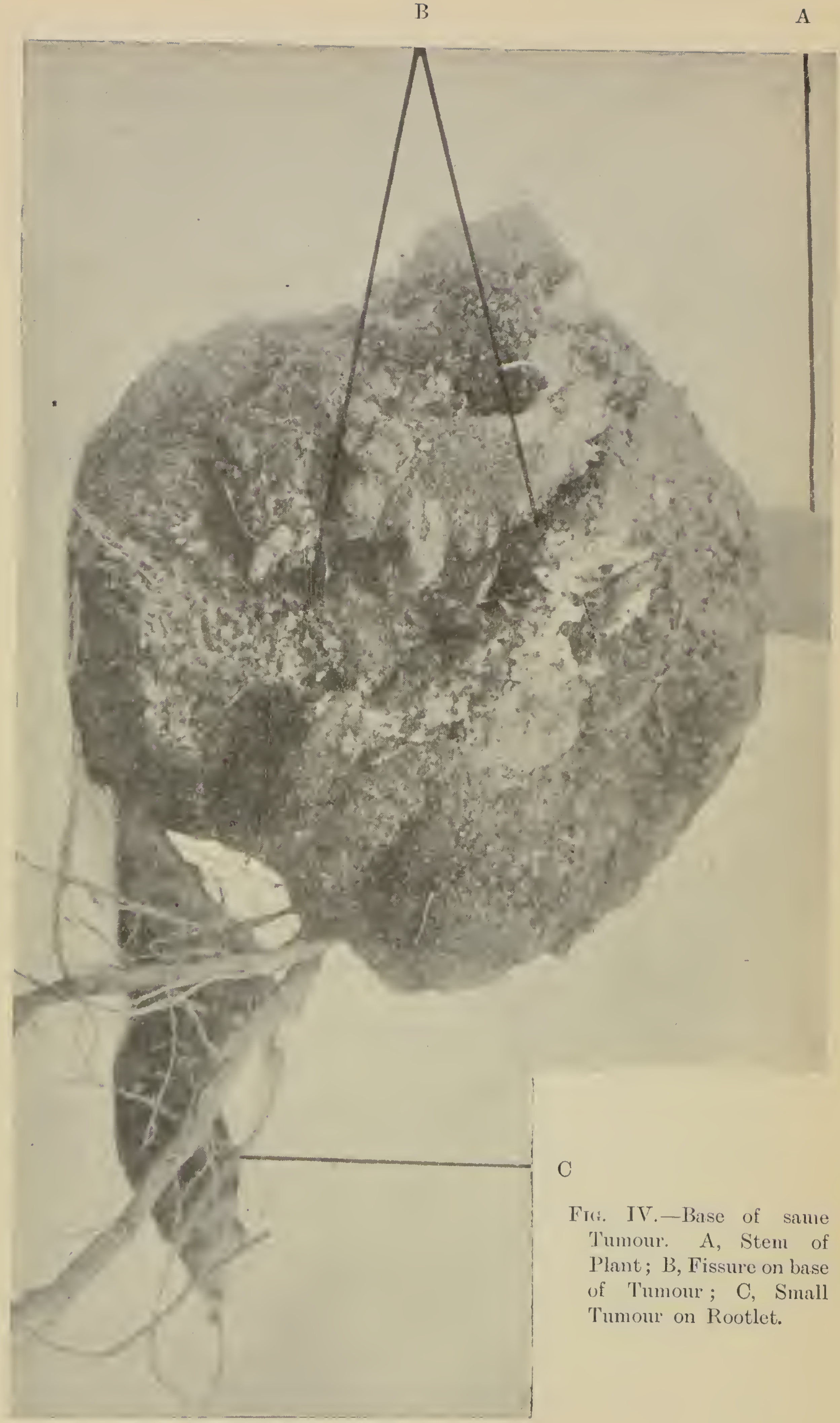


Fig. IV.—Base of same Tumour. A, Stem of Plant; B, Fissure on base of Tumour; C, Small Tumour on Rootlet.

successive phases of a parasite of this class. Both organisms were extremely difficult to stain; ordinary staining methods were found to be useless for the purpose, and special complicated staining processes had to be devised. Full details of these will be found in the paper itself. No one who compares in Fig. VI. the fourteen phases referred to can fail to be impressed by the marvellous similarity of A, *Plasmodiophora brassicæ* and B, the organism called

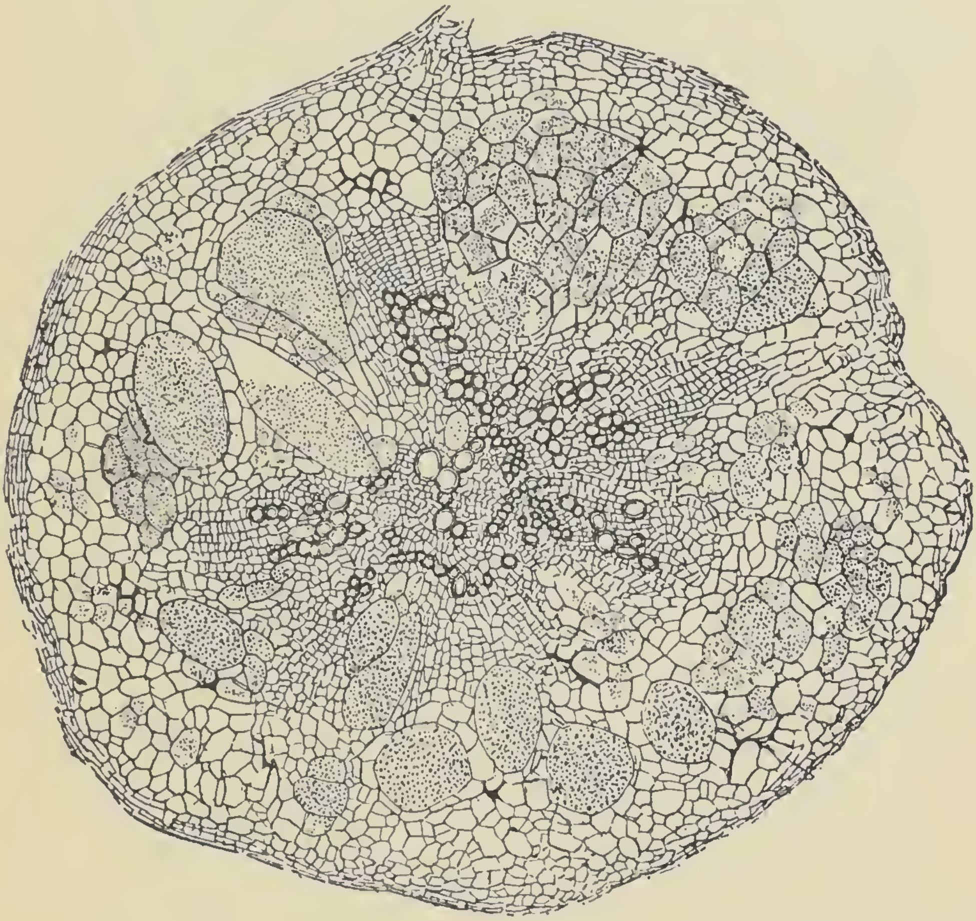


Fig. V.—Transverse Section of a Root Attacked by *Plasmodiophora*. Numerous giant-cells are seen full of granular protoplasm: these enlarged cells disturb the arrangement of the other tissues, and act as centres of attraction to food-supplies. (After Woronin.)

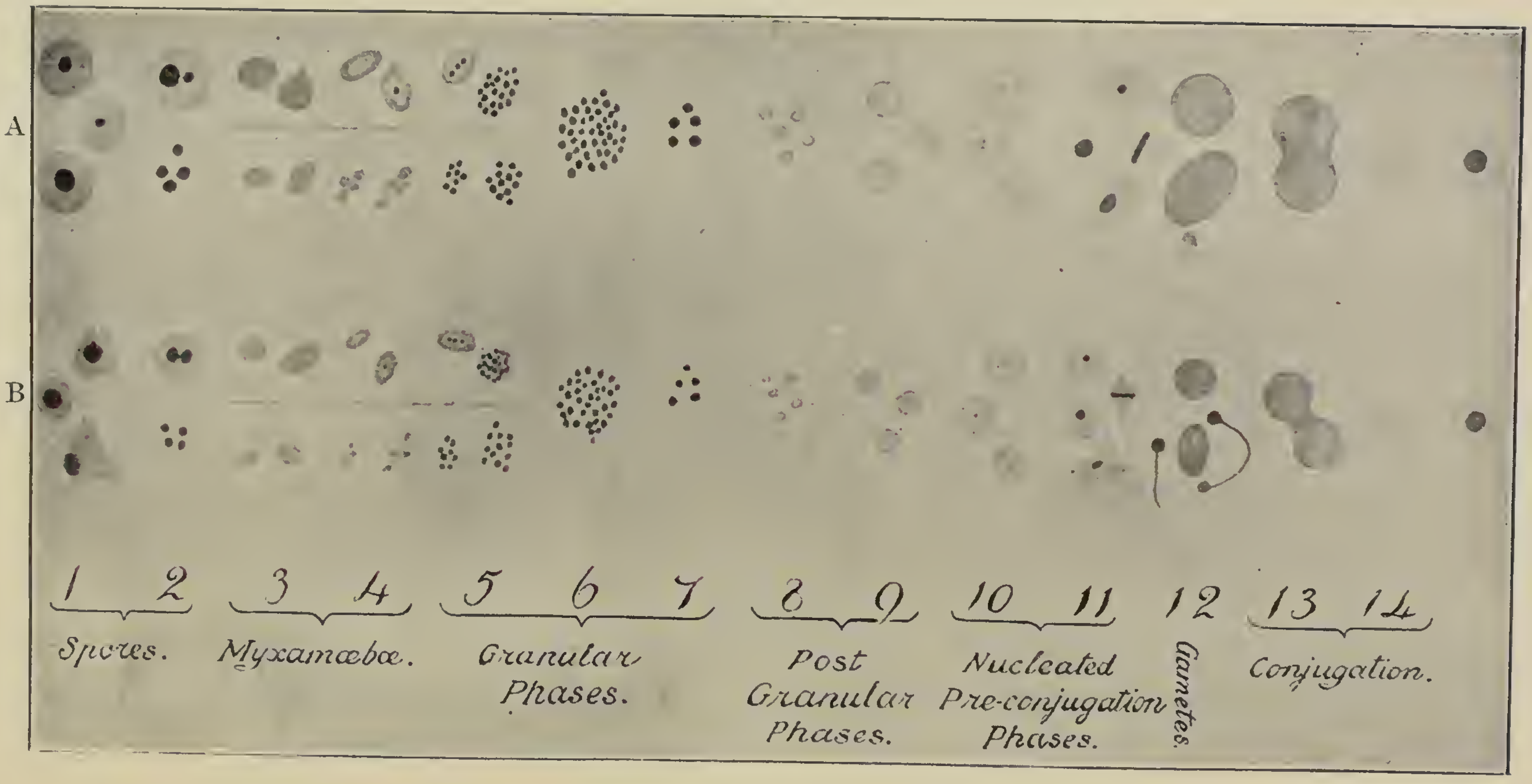


FIG. VI.—A, *Plasmodiophora brassicæ* ; B, *Plasmodiophora carcinomatis* (Ford Robertson and Wade).

by the authors *Plasmodiophora carcinomatis*, and developed by them from carcinomatous tissue.

While many observers have detected organisms corresponding to stages in a similar life-cycle in malignant tumours, *e.g.* Russell's bodies and Plimmer's bodies, none have shown anything like this which differs from that of others in the recognition of the granular and post-granular stages.

The life-cycle of *Plasmodiophora brassicæ* is one of the strangest things in nature and resembles to some extent that of the malaria parasite. Indeed some biologists suggest that the malaria parasite belongs to the same class, viz. the mycetozoa, of which the greater number belong to the subdivision myxomycetes or slime moulds (the myxogasteres of Fries).

These slime moulds are difficult to place.

If the hypha is the morphological test of a fungus, then it is plain that the slime moulds are not fungi. No myxomycete has hyphæ or anything of the kind.

The fungi, however, are incapable of independent existence, being destitute of chlorophyll. In this respect the slime moulds are like the fungi; with the exception of Plasmodiophora, which is a parasite, they are nearly all saprophytes. All are destitute of chlorophyll. This physiological character is one which the fungi share with the whole animal world. That their amœboid spores and plasmodia ally them at once to the amœba is the position suggested by De Bary in 1858, and adopted since by many distinguished authorities, among whom may be mentioned Saville Kent and Dr. William Zopf (*Die Pilzthiere*, 1885). Rostafinski, who was a pupil of De Bary's, and whose monograph on the slime moulds was written under De Bary's supervision, adopts the title "Mycetozoa," suggested by his

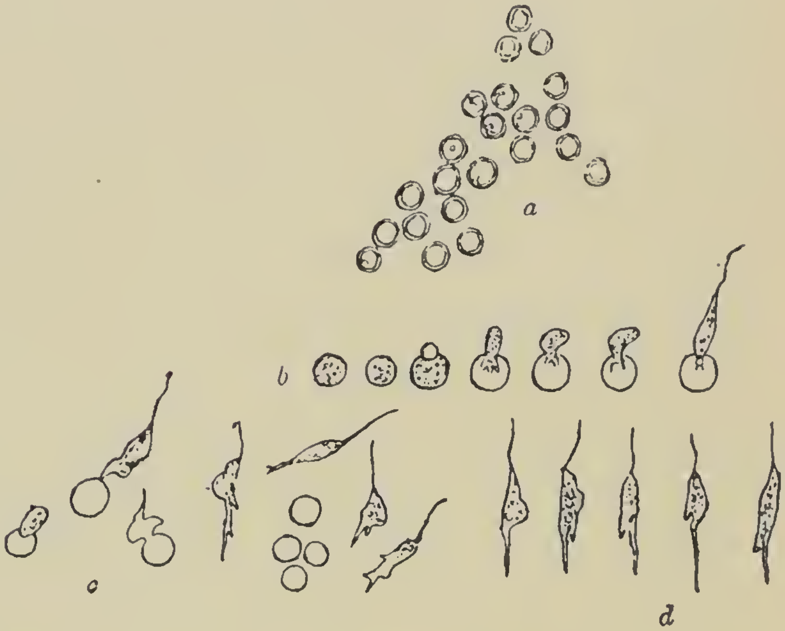


Fig. VII.—Spores of *Plasmodiophora brassicæ*, showing Various Stages of Germination. The spore (*a*) bursts as one point (*b*), and the protoplasmic contents emerge as a ciliated myxamœba (*b*, *c*, *d*), which creeps about by continually changing its form (*d*). Very highly magnified. (After Woronin.)

master as indicating a closer relationship with the animal world, but really has little to say in regard to the matter.

In the course of their life-history the myxomycetes present two very distinct phases—the vegetative phase and the reproductive. The vegetative phase differs from that of all other plants, since the organism then consists of a simple mass of protoplasm destitute of cell-walls and in all respects an amœba. In this state the myxomycetes affect damp and moist situations. They are found in soil, on piles of rotten leaves, in straw, and especially in the wet tissues of decayed wood.

The vegetative phase unquestionably justifies, so far, the views of those systematists who would place them among the animals. It may last for months, possibly for years, when the reproductive phase at length arrives and spores are formed, which germinate and pass through a regular life-cycle, ultimately to reach the amœboid condition again.

The life-cycle of a typical mycetozoan is illustrated on page 20 (Fig. VIII.). It will be seen from page 16 that the life-cycle of *Plasmodiophora brassicæ* differs considerably from this. Indeed the life-cycle of *Plasmodiophora brassicæ* differs so greatly from the typical mycetozoa that De Bary places it in a class by itself among doubtful mycetozoa (De Bary, p. 446). In Macbride's *North American Slime Moulds* it is given a subclass by itself as phytomyxinæ, as the only purely parasitic form.

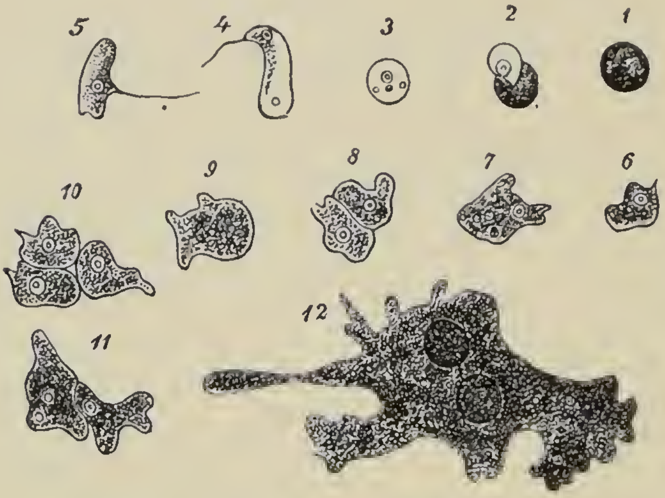


Fig. VIII.—*Chondrioderma difforme.* 1. Ripe spore. 2. The same germinating. 3-5. Swarm-cells. 6, 7. The same in the amœboid state. 8. Two amœboid swarm-cells in close contact. 9. The same when coalesced to form the beginning of a plasmodium. 10. Three swarm-cells in contact with one another. 11. Two of them after coalescence, the third still free. 12. Young plasmodium, which has taken up two spores into its substance. (After Cienkowski, from Sachs' *Lehrbuch.* Magn. 350 times.)

After reading an enormous mass of literature on the subject, I am convinced that there is every indication that cancer may be of parasitic origin. If it be parasitic one is driven to the conclusion that it must be due to an organism of this class which undoubtedly induces malignant growths in plants to such an extent that in certain cases the cells of the host become its own parasite.

CHAPTER II

THE OCCUPATIONAL INCIDENCE

If then cancer be due to a parasite akin to the myxomycetes, it seemed interesting to inquire into what was known regarding the physiology and metabolism of such organisms and to discover whether there were any conditions in the trades showing the highest cancer death-rate which would encourage the growth of such a parasite.

Unfortunately very little is known regarding their conditions of life. Some work has been done in America and in certain agricultural colleges, but, as has been said, the entire group has been rather neglected owing to many zoologists considering them plants and many botanists animals.

Pfeffer in his *Plant Physiology* (vol. ii. p. 121) states that a concentration of the external medium without any change in its composition causes them to produce perennating bodies, which are specially resistant to drought; that certain of them show a positive chemotactic movement towards extract of tan; that the spores of certain are attracted, especially by lactic, butyric and malic acids; that their plasmodia are killed by exposure to light of moderate intensity, even feeble illumination distinctly retarding the amœboid activity and also the streaming of the endoplasm.

As to their nutrition, all that De Bary can say is, that they "live on organic substances, of course with the necessary ash constituents, and what definite chemical substance does actually and usually serve or is fitted to serve as nutrient material to the myxomycetes is a question which has not yet been thoroughly examined." This is practically all that I have been able to discover.

When so little is known regarding the entire group of organisms known as myxomycetes, it is small wonder that so much obscurity exists regarding the small subclass which, as I have said, is parasitic and not saprophytic like all the others.

Agriculturists, however, have suffered severely from the ravages of Plasmodiophora and one fact in particular is given in agricultural text-books as the result of their practical experience, viz. that whenever manures are used which have been *dissolved in sulphuric acid* the disease is almost certain to occur. This fact seems very important. Of its accuracy there can be no doubt, since the Board of Agriculture goes so far as to distribute leaflets gratis all over the country warning farmers that manures dissolved in sulphuric acid have a marked tendency to encourage the disease.

It is obvious, therefore, that such manures have a stimulating effect upon Plasmodiophora. How they may act will be dealt with later. At present one would, as has been said, inquire into the conditions in the trades showing the highest cancer death-rates in the endeavour to see whether there were anything in these conditions which would favour the growth of such a parasite on these lines.

The last complete returns of the Registrar-General were issued in 1908 and covered the period from 1900 to 1902. The comparative mortality figure from cancer in the various trades is given as follows. It is difficult to understand the system of selection of the trades which has been made, but they are given as published.

Occupation.	Comparative Mortality Figure from Cancer.
Chimney-Sweep	136
Inn-, Hotel-Servant (London)	133
General Labourer (Industrial Districts)	116
Brewer	112
Furrier, Skinner	111
General Labourer	111
Seaman, etc., Merchant Service	103

Occupation.	Comparative Mortality Figure from Cancer.
General Labourer (London)	102
Tinplate Manufacturer; Tinplate Goods Maker	95
Domestic Coachman, Groom	94
Innkeeper, Servant, etc., in London	94
Inn-, Hotel-Servant	88
Chemical Manufacture	85
Lead Manufacturer; Leaden Goods Maker	82
Indiarubber, Gutta-Percha Worker; Waterproof Goods Maker	82
Bottle-Maker	82
Wood Turner, Cooper, etc.	80
Textile Dyer, Bleacher, Printer, Finisher, etc.	79
Tramway Service	79
Costermonger, Hawker, etc.	79
Messenger, Porter, etc. (not Railway or Government)	79
Lace Manufacture	79
General Shopkeeper	78
Cabinetmaker, etc.	75
Bargeman, Lighterman, Waterman	75
Coal-Miner	51
Silk, Satin, Crape, etc, Manufacture	51
Saddler, Harness-Maker	51
Farmer, Grazier, Farmer's Son, etc.	51
Brush-, Broom-Maker; Hair-Bristle Worker	51
Schoolmaster, Teacher	49
Inn-, Hotel-Servant (Industrial Districts)	49
Clergyman, Priest, Minister	48
Agriculturist	48
Platelayer, Railway Labourer; Navvy, etc., Road Labourer	48
Gardener, Nurseryman, Seedsman	48
Railway Engine-Driver, Stoker	48
Farmer, Grazier, etc., in Agricultural Districts	46
Coal-Miner (Monmouthshire and South Wales)	46

Occupation.	Comparative Mortality Figure from Cancer
Farm Labourer, Farm Servant	45
Coal-Miner (Lancashire)	44
Agriculturist in Agricultural Districts	44
Coal-, Coke-Merchant, Dealer	44
Labourer, etc., in Agricultural Districts	42
Coal-Merchant; Coke-Burner, etc.	42
Lock-, Key-, Gasfittings-Maker; Gasfitter	41
Wheelwright	40
Copper Miner	39
Paper Manufacturer	39
Copper Manufacturer, Worker; Coppersmith	39
Tanner	33

It is interesting to compare this table with a previous one which was issued about twenty years ago and which is printed below.

Occupation.	Comparative Mortality Figure from Cancer.
Chimney-Sweeps	156
Innkeepers in London	70
Brewers	70
Inn and Hotel Servants	65
Commercial Travellers	63
Maltsters	61
Merchant Seamen	60
Lawyers	60
Gas Workers	59
Tool and Scissors Makers	58
Coachmen and Grooms	58
Butchers	57
Coal-Heavers	56
Innkeepers	53

Occupation.	Comparative Mortality Figure from Cancer.
Plumbers	53
Tobacconists	51
Dock and Wharf Labourers	51
Shoemakers	50
Drapers	49
General Labourers	48
Porters	48
Fishermen	46
Blacksmiths	45
Medical Practitioners	43
Fishmongers	42
Farmers	36
Coal-Miners	36
Potters	35
Clergy	35
Grocers	34
All unoccupied males	96
All occupied males	44

Two striking facts are shown by a comparison of these tables: (1) That the chimney-sweep has by far the highest mortality figure of all trades and (2) that in the first and later table the percentage of the chimney-sweep has decreased while that of all other trades has increased. In the last published report of the Registrar-General, this decreasing cancer mortality of chimney-sweeps is specially referred to and it is also stated in Table 7 of the report that ever since 1860 the mortality in this occupation has declined continuously to such an extent that the present figure is only two-thirds of what it was at that date.

Now, whatever bearing it may have upon this point, it is certainly an interesting fact that the year 1840 marked the passing of the Chimney-Sweepers and Chimney Regulation Act which forbade any person to allow a child or young person under the age of twenty-one to ascend or descend a chimney or enter a flue for the purpose of sweeping or coring the same, as had previously been the regular custom. This Act was made more stringent in 1864. It forbade a chimney-sweeper even to bring a young person into a house with him. Previous to this period, house chimneys had been built wide and square in order that children might clean them in this way. Afterwards, when they had to be swept with brushes, it was found that the round chimney was more easily cleaned and the present narrow clay tube chimneys came gradually into invariable use. The old chimney with its rough stone-and-lime surface must have been considerably dirtier than the modern one.

Whether this point has any bearing or not upon the decreased death-rate among sweeps, there is no doubt that in the text-books soot is said to cause epithelioma, by irritation, presumably mechanical. This, however, is not a satisfactory explanation, since the disease is rare among working coal-miners, whose skins are saturated with carbon in the shape of coal dust, which should be equally irritating.

Although the mechanical irritant theory is not satisfactory, there is no doubt whatever that soot, or some product of combustion, is an active agent.

Ordinary coal soot has a deleterious effect upon the leaves of plants, and this was formerly ascribed to mechanical irritation or to the blocking of the stomata through which the plants breathe. Stockhardt, however, proved this to be wrong by an experiment, eighty-six times repeated, in which he filled a glasshouse with an atmosphere of soot from burnt benzine so thick that the contours of the plants could not be seen, and that the leaves were almost black. No disturbance of growth could be detected, and the leaves were afterwards as fresh as those outside. The pure carbon soot from the benzine had no effect, while coal soot had.

In a similar fashion the carbon in coal does not cause cancer in the miner, while the soot affects the sweep.

The fact that coal soot has some relation to the sweep's high mortality is also, I think, indicated by the part of the body chiefly affected, as shown by a table in the Registrar's latest report. This table shows that in 30 per cent. of the deaths the scrotum and its adjacent parts are those affected. Now the face of a working sweep will always be found to be covered with light powdery soot, while his hands and nails are absolutely black and coated. The extremities are not liable to malignant disease, but these soot-engrained hands must for obvious reasons several times in a working day come in contact with the susceptible parts which are associated with "sweep's cancer."

At one time I thought it possible that scrotal cancer might be caused by proximity to the fumes from chimney heads when working, as these would be on the same level approximately as the sweep's scrotum. This idea, however, is negatived by the facts that scrotal epithelioma occurs in guano workers and that in the report of the Royal Commission appointed to inquire into the condition of boys who used to clean chimneys by climbing up them, there is medical evidence to the effect that boys of tender years were operated on for scrotal cancer.

An additional proof that the disease is fostered by a product of combustion is the Kangri basket with which the natives of Kashmir warm themselves in winter. This is a basket containing a clay pot in which burning coal or charcoal is placed and is worn next the skin under the clothes. Enormous cancers develop upon the abdomens of many of the wearers. A surgeon who has both seen and operated on these unique malignant tumours informed me that it was only when the basket portion was destroyed and the sooty clay came in contact with the skin that the disease arose.

If soot, then, be an active agent in producing malignant disease, as is shown by the appalling mortality among chimney-sweeps and by other indications, while coal-dust has no effect upon the coal-miner, it is obviously of importance to consider what soot contains which coal does not.

Coal soot is chiefly composed of finely divided carbon, but it also contains a considerable proportion of sulphate of ammonia. Coal contains sulphur and nitrogen, and in the process of combustion ammonia and sulphurous acid are evolved, which combine to form the above-named salt. It is the existence of sulphate of ammonia in large quantities in soot that has led to its use as a fertiliser by farmers and gardeners.

Here, however, a difficulty presents itself. If, by the above process of reasoning and of elimination, one is led to the conclusion that sulphate of ammonia or the sulphurous acid which goes to compose it is an etiological factor, how are we to reconcile this result with the fact that paraffin has induced among paraffin workers cancerous growths in several well-authenticated cases. This for a long time puzzled me, but I have at last hit upon a probable solution. I was at first led astray by the fact that the chief source of commercial sulphate of ammonia is mineral oil works, but this cannot affect the question, as ammonia water is the only real by-product, and the sulphuric acid necessary to combine with this and form the ammonium sulphate is bought in and added in a separate department of the works, having no connection with refined paraffin.

The puzzle was to find whether there was anything in common between commercial paraffin and soot. When we examine the practical methods of paraffin refining we find that in order to remove the oily bases it has been found in practice that an acid treatment of the finished oil is necessary. It is not possible to remove the whole of these bases by one or even two acid treatments, but the oil must be *shaken up with acids a number of times.* All kinds of acids have been tried, but the results of numerous experiments have proved *sulphuric acid* to be the only one suitable for this work. It is specially pointed out in ' Redwood's *Mineral Oils* as of the utmost importance that all such sulphuric acid treated oils must be allowed to settle until as thoroughly freed from this acid tar as possible.

In removing the impurities the sulphuric acid must form various sulpho-acids, but it is difficult to see how, except mechanically, any of such mixture of sulpho-acids could be present in the paraffin after the operation. It would be a difficult matter to say what were the sulpho-acids, as there might be, of course, fifty different varieties, entirely depending on what the impurities were. There would certainly be no sulpho-acids of the paraffin itself, as this remains unacted on, and it is only impurities that are acted on.

One impurity which is bound to exist, however, is ammonia — since the method of separation of ammonia water from the crude oil is a very rough and ready one—and we are driven to the result that even in refined paraffin, as in soot, sulphate of ammonia and sulpho-acids must often exist.

When the mortality figure tables of the Registrar-General are scrutinised in the light of these facts there are several curious corroborations in the conditions affecting the other trades most liable to malignant disease which may be mentioned here.

I propose to take the highest of these in order and state facts which I have elicited after a good deal of trouble.

Brewer.—It has been abundantly proved that the consumption of alcohol has no connection with cancer, and accordingly the brewer's high mortality rate is extremely interesting. The brewer's work is conducted among wort boilers and other vessels heated by fire and so constructed that the maximum of flame may get round them. The lower flues are generally horizontal, and many interstices permit and encourage the accumulation of soot.

The mortality figure of brewers has also greatly increased in recent years. I have examined breweries and brewing methods most carefully in the endeavour to discover the cause of this. One curious fact I have elicited is that the caramel which is used to colour all beers was formerly only made from burnt sugar, but in order to make the substance tasteless it is now prepared by charring the sugar with sulphuric acid. The brewer is also constantly handling "sulphured" hops. The object of sulphuring hops—that is, using sulphur with the fuel when drying hops—is to bleach them and make them brighter. The sulphur itself in the hops, and therefore in the beer, exists as *sulphurous acid* (Moritz and Morris, *Science of Brewing*, p. 199).

Again, in nearly all beers antiseptics are now used, the one in almost universal use being bisulphite of lime, which is prepared by saturating a solution of sulphite of lime with sulphurous acid. It is sometimes used in the mash, sometimes in the copper, but much more frequently in the finished beer. Other sulphites used are sulphite of sodium, sulphite of potassium, sulphite of magnesium, etc. The only substance other than a sulphite which is at all largely employed is salicylic acid (Moritz and Morris).

Furrier and Skinner.—It is a very strange and instructive fact that the furrier should be almost at the top of the list while the tanner is at the bottom. The cause must be due to some difference in the methods of preparing skins for furs and for leather. In the former case the hair must be preserved, in the latter entirely removed. The tanner steeps his hides in lime, which, as will be shown later, is apparently prophylactic, while the furrier and skinner adopts a different process. The skins of mammals, we are told (*Ency. Brit.*, xxiii. p. 90), are best preserved by a mixture of 4 parts burnt alum to 1 part of saltpetre. Alum, it must be remembered, is composed of sulphuric acid, alumina, an alkali, and water. Nearly all furs have also to be dyed, and the mordant used is chiefly sulphuric acid.

Seamen have shown a great increase in their cancer mortality, due apparently to the increase of steamers and the decrease of sailing ships. The fact that they have a higher mortality figure than fishermen seems to me to be due to this and to their stuffy and smoky quarters. Fishermen do not so often sleep on board; indeed the greater number never do.

Tinplate Manufacturer.—What element in the manufacture of tinplate can cause this very high mortality figure? If my theory is correct, this would explain it: "Before 'tinning,' the plates are called black plates. When the iron has been cut to the required size the plates are 'pickled,' *i.e.* they are immersed in hot sulphuric acid."—*Chambers's Ency.*, x. p. 217.

Chemical Manufacturers.—The intimate connection of these trades with sulpho-acids is at once obvious.

Lead-workers.—Here we have a close connection with sulphurous acid. It is pointed out in the last Report of the Registrar-General that the mortality of lead-workers had decreased since 1890. Now, until recent years only a small quantity of lead was obtained from any other ore than galena, which is a sulphide of lead. When galena is smelted, much of the sulphur goes to form sulphurous acid, which escapes as a gas. There remain in the hearth of the furnace oxide, sulphate, and sulphide of lead, which react upon each other, forming sulphurous acid and metallic lead.

Indiarubber-workers.—The connection here is at first sight obscure, but the fact remains that alum and sulphuric acid are constantly used to effect the coagulation of the juice, and it is pointed out in the *Ency. Brit.* (Indiarubber) that traces of these remaining in the rubber constantly work mischief in it.

Occupations in London.—Nearly all the occupations "in London" for which a figure is given are higher than those elsewhere. This is probably due to the enormous amount of both acids in the air of London. This excess has been often pointed out.

X-ray Workers.—In this imperfect survey of the trade and occupational incidence of the disease I would venture to make a suggestion regarding what is called X-ray cancer, which so commonly follows a dermatitis on the hands of X-ray workers.

It is certainly one of the most puzzling aspects of the whole cancer problem that X-rays should cure rodent ulcer and yet induce epithelioma on the fingers of the operators of these rays.

If, as stated before, the plasmodia of myxomycetes are killed by exposure to light of moderate intensity, it is quite intelligible that X-rays should cure cancer, but quite unintelligible that they should cause it.

The X-rays admittedly cause a dermatitis and thereby diminish the resistance of the epithelium. It should not be forgotten, however, that most X-ray operators have to prepare many skiagraphs and to develop negatives. This, in my opinion, is the cause. Fixing plates by means of hypo-sulphite with fingers, the skin resistance of which is already weakened, is much more likely to cause the epithelioma than the rays themselves. These would only indirectly be concerned.

Guano-workers.—In the new edition of Bryant and Buck's *Surgery* it is stated that scrotal cancer nowadays is found among workers in guano as well as among chimney-sweeps and coal-tar workers. This seems inexplicable until one realises that the richest deposits of guanos have been largely worked out, and that the stores now largely drawn upon are in many cases compact and rocky in texture, and require now to be disintegrated and treated with sulphuric acid (*Encyclopædia of Agriculture*, vol. ii. p. 287).

I can only say that if sulphurous acid or sulpho-acids have no connection with cancer I have stumbled across an extraordinary series of coincidences.

Coal Tar Workers.—It has long been known that workers in coal tar and creosote were especially liable to epithelioma, and the Home Office has recently added a new interest to the subject by the issue of proposed regulations regarding workers with gasworks tar pitch, in which the interesting exception is made that these rules are not to apply to workers in *blast furnace* tar pitch, since Dr. Whitelegge, the chief inspector of factories, could not find similar cancerous conditions among the workers in blast furnace pitch (*British Medical Journal*, April 15, 1911, p. 885). This observation coming from so high an authority is of great interest and importance from the point of view of cancer research.

If gasworks tar pitch causes cancer and blast furnace tar pitch does not, it is clearly of importance to compare their composition.

Blast furnace tar is altogether different from ordinary gas retort tar and cannot be employed for the same purposes.

Most blast furnaces are, of course, fed with coke from which no tar can be got. In the West of Scotland, however, a coal is got which is suitable for furnace purposes. The tar from this is not obtained from retorts but condensed from the enormous volume of gas issuing out of the blast furnace throat. This gas is carried to a separate plant and in nearly all cases is treated by the Gartsherry process which consists in simply cooling it down and washing it with water. The result is a pure tar in which even anthracene cannot be detected, and in which there is a much larger proportion of phenols than is obtained in gas coal tars.

Coal tar pitch made in gasworks, on the other hand, is an extremely complex mixture of chemical compounds some of which have not yet been even isolated. It contains nitrogenous compounds chiefly of a basic nature and *sulphur compound*s derived from the pyrites, etc., never absent in coal.

Free sulphur has been found by Kehlstadt in the distillates of coal tar. Lunge considers it is formed from SO_2 and H_2S under the action of water.

There must also always be present in coal tar :—

Hydrogen Sulphide H_2S.
Ammonium Sulphide $(NH_4)_2S$.
Ammonium Sulphocyanide $(NH_4)NCS$.
Sulphur Dioxide SO_2.

LUNGE, p. 225.

Carbon Bisulphide CS_2 has also been found in as great quantity as 6 per cent. by Watson Smith in the first runnings of benzol from London gas tar, while Greville prepared it on a large scale from the purifiers.

Carbon Oxysulphide COS is, according to Lunge, bound to exist.

C_4H_4S, C_5H_6S and many sulphuretted bodies have also been found.

It is obvious, therefore, that many sulphur compounds exist in coal tar pitch which are not to be found in blast furnace tar pitch, and it must further be borne in mind that, according to the Alkali Inspector's reports, 95 per cent. of the gasworks pitch made in England is sold in the medium hard stage after distilling up to hard pitch and *softening it with creosote oil.* It is also revivified by means of creosote oil. Now creosote oil is in itself a cause of cancer, and Lunge (*Coal Tar*, p. 523) indicates that its unpleasant and nauseous smell is due to sulphur compounds not yet isolated.

We are thus driven to the conclusion that the difference between blast furnace tar pitch which does *not* induce epithelioma and gasworks tar pitch which *does* is chiefly the sulphur compounds contained in the latter, and also in the creosote oil which is used to soften it.

CHAPTER III

THE LOCAL INCIDENCE

It has been argued on the theory of probabilities that the so-called cancer houses do not exist. However this may be, it is unquestionable that there are most striking topographical variations in the incidence of the disease. In proof of this it is unnecessary to refer to the various papers and reports which have been prepared on various parts of the country in view of the fact that we again have the figures of the Registrar-General to deal with.

These figures, showing the percentages for the whole of Scotland for the three years 1895, 1896 and 1897, will be found in the *Edinburgh Medical Journal* for January 1903, page 23, in a most valuable article by Dr. W. G. Aitchison Robertson, who took the trouble to correct them by allocating to their own places of residence patients who had been removed to hospitals and infirmaries for treatment and had died there.

As Dr. Robertson points out, at present our only means of treating the disease is by surgical interference, and consequently a large proportion of cancer cases are sent to hospitals or infirmaries in the large towns for operation. Many of these patients die away from their usual places of residence and in this way the mortality from cancer is unduly raised in many towns, while the reverse holds as regards country districts.

In order to counteract this registration error Dr. Robertson personally visited the larger institutions in Edinburgh and in other large towns in Scotland, extracted from their registers all the patients who had died from cancer in these institutions during the years in question and apportioned them to their proper towns and counties. This examination must have involved an enormous amount of labour, but the result is a set of statistics of great value, and the tables are appended—

Table showing the Percentage of Cancer Deaths, as Calculated from the Returns of the Registrar-General for Scotland (first column), and as Corrected. **The average for the whole of Scotland for the three years, 1895-6-7 was 4·023 per cent.**

	Registrar-General.	Corrected.		Registrar-General.	Corrected.
Principal Towns—			*Principal Towns—* contd.		
Glasgow . .	3·12	2·98			
Edinburgh . .	5·15	4·03	Paisley . .	3·16	3·2
Dundee . .	4·17	4·09	Greenock . .	3·04	3·12
Aberdeen . .	4·65	4·53	Coatbridge . .	2·69	...
Govan and Partick	2·65	2·8	Perth . . .	4·06	4·29
Leith . . .	3·87	4·11	Kilmarnock .	3·80	...

	Registrar-General.	Corrected.
Large Town Districts—		
Inverness	5·02	5·25
Peterhead	2·79	...
Arbroath	4·76	...
Forfar	7·02	...
Montrose	5·71	...
Dunfermline	3·64	3·93
Dysart	4·10	...
Kirkcaldy	5·21	5·81
Alloa	2·45	...
Falkirk	2·64	...
Stirling	4·12	4·19
Dumbarton	1·81	...
Kirkintilloch	1·75	...
Old or West Kilpatrick	2·80	...
Eastwood (Landward)	3·11	...
Port-Glasgow	3·86	...
Ayr	4·83	...
Cambusnethan	2·99	...
Dalziel	2·29	...
Kinning Park (Landward)	1·76	...
Hamilton	2·48	...
New Monkland	2·36	...
Rutherglen	1·93	2·14
Galashiels	5·19	...
Hawick	4·86	5·27
Dumfries	4·56	4·61
Small Town Districts—		
Shetland	3·33	...
Orkney	3·42	...
Caithness	4·49	...
Ross and Cromarty	4·80	...
Nairn	4·11	...
Elgin	3·92	...
Banff	4·88	...
Aberdeen	4·75	...
Kincardine	4·44	...
Forfar	5·86	...
Perth	6·26	...
Fife	3·74	...
Small Town Districts—contd.		
Clackmannan	2·39	...
Stirling	2 66	...
Dumbarton	4·23	...
Argyll	5·28	...
Bute	4·09	...
Renfrew	3·82	...
Ayr	3·80	...
Lanark	2·70	...
Linlithgow	2·62	...
Edinburgh	3·78	...
Haddington	5·05	5·13
Berwick	4·85	...
Peebles	5·30	...
Selkirk	5·11	5·46
Roxburgh	6·68	...
Dumfries	5·65	...
Kirkcudbright	4·65	...
Wigton	4·20	...
Mainland Rural Districts—		
Caithness	5·49	5·84
Sutherland	4·49	4·61
Ross and Cromarty	5·21	5·24
Inverness	4·98	5·39
Nairn	8·77	9·73
Elgin	5·78	5·96
Banff	6·48	6·63
Aberdeen	5·29	5·37
Kincardine	4·32	4·54
Forfar	6·87	7·73
Perth	5·34	5·71
Fife	5·05	5·61
Kinross	5·06	5·96
Clackmannan	5·12	5·51
Stirling	3·21	3·90
Dumbarton	6·26	7·37
Argyll	4·98	5·53
Renfrew	4·03	4·40
Ayr	2·95	3·15
Lanark	3·78	4·18
Linlithgow	3·50	4·48
Edinburgh	4·13	4·95
Haddington	4·25	5·59

	Registrar-General.	Corrected.		Registrar-General.	Corrected.
Mainland Rural Districts—contd.			*Insular Rural Districts*—		
Berwick . .	6·40	6·40	Shetland . .	2·91	3·73
Peebles . .	4·68	5·07	Orkney . .	4·91	5·32
Selkirk . .	4·29	6·60	Ross and Cromarty	3·20	...
Roxburgh . .	6·65	7·05	Inverness . .	2·93	...
Dumfries . .	6·49	6·70	Argyll . .	4·55	...
Kirkcudbright .	5·18	5·84	Bute . . .	7·61	...
Wigtown . .	6·52	6·67			

Taking a broad view of these figures, it will be seen that the percentage varies from 1·76 in Kinning Park, a suburb of Glasgow, and 1·75 in Kirkintilloch, to 9·73 in the rural districts of Nairnshire. The differences cannot be due to food, as they are too widespread: they cannot be due to urban life, since many of the towns have the lowest mortality.

One point may also be mentioned at once as controverting the very generally accepted idea that the proximity of tall trees has some connection with cancer. It will be seen that the rural districts of Orkney have a mortality above the average, amounting to 5·32, and as there is only one tree of any size in Orkney, which is looked upon as a curiosity and is situated in the centre of Kirkwall, it is obvious that the tree theory falls to the ground.

In view of these tables, I have motored over practically the whole of Scotland in the endeavour to find any clue to these pronounced differences.

On examining the COUNTIES, none of the ordinary theories which have been put forward, such as proximity to rivers and flooded districts, seemed applicable ; but one thing has impressed me very strongly, viz. *that those where the death-rate was low were comparatively flat, or at most had low, swelling, undulating hills, with houses built on their sides, whereas those where the mortality was high were intersected with gulleys and valleys, with the houses as a rule situated in the hollows.*

To take, for example, the county showing the highest death-rate in Scotland, viz. the rural districts of Nairn, with a mortality of 9·73 : the inhabited part of this county is largely made up of deep valleys with wooded sides, and the houses in the hollows. As one traverses it from south to north, however, about four miles from the sea the land slopes down to a perfectly flat stretch of country, at the extremity of which is the town of Nairn, where the mortality drops, as will be seen, to 4·11.

A very similar case is that of Dumbartonshire, which has a mortality, as will be seen, of 7·37. The county itself is very rough and hilly. The town, on the other hand, is situated on a wide flat beside the Clyde.

As the *Ordnance Gazetteer* says, its site is "a low flat plain." The mortality figure of the town is only 1·81, as compared with the 7·37 of the entire county.

Other instances might be given, but it is dangerous to draw equally accurate inferences from the mortality figures of any but the principal towns and the large town districts. One may generalise on the configuration of a county after having traversed it in several directions. The small town districts, on the other hand, are generally made up of several little villages spread over the whole county and occupying sites of a very diverse nature. In the case of these principal towns and large town districts, however, I have found a most interesting set of conditions, and feel justified in saying that I have practically proved that the situations have a marked connection with the percentage of cancer deaths.

I have taken all of the principal TOWNS AND LARGE TOWN DISTRICTS except Montrose, the situation of which is exceptional, and have grouped them, after careful consideration and in most cases personal examination, into four classes of sites, viz. the towns lying in a cup or hollow; the towns occupying a flat site and with comparatively flat surroundings; the towns on distinctly steep or hilly sites; the towns built on gentle slopes. The results are appended. After each town its corrected percentage of cancer deaths as shown by Dr. Aitchison Robertson is given, and in order that my own classification may have some proof, I have printed opposite each a description of the site as given in the *Ordnance Gazetteer* for Scotland. This will enable those who are not familiar with the districts to check my grouping. The words printed in italics are taken from the *Ordnance Gazetteer*. Any remarks in ordinary type are my own.

Towns Lying in a Pronounced Hollow and Showing a High Cancer Death-Rate.

Forfar.	7·02.	*The town stands* 200 *feet above sea-level in a kind of basin formed by the surrounding slopes.*
Galashiels.	5·19.	*The town sends off-shoots, extending up the slopes to the adjacent hills. It is flanked and overlooked on the one side by Meigle Hill* (1387 *feet*) *and Gala Hill, and on the other side Buckholm and Langlee Hills.*
Hawick.	5·27.	*The town is in a basin.*
Kirkcaldy.	5·81.	This town lies in a cup, and, at the same time, on a steep slope. *The main street stretches like a skeleton backbone that has been twisted with spinal curvature, while side streets and closes lead down to the shore or back to the villas which adorn the upper part of the town.*
Inverness.	5·02.	*On all sides, except the sea margin, the site is hemmed in by rising grounds.*

Towns Lying in a Less Pronounced Hollow Showing a Somewhat Reduced Death-Rate, but still Above the Average.

Aberdeen.	4·53.	This city lies in a hollow at the mouth of the River Dee.

Ayr.	4·83.	*Its site is low ground, screened all round by gently rising heights which form a great natural amphitheatre.*
Perth.	4·29.	*The site of the town is a flat-bottomed hollow environed with rising ground overlooked by an amphitheatre of well-wooded hills.*
Arbroath.	4·76.	*Its site is a little plain engirt on the land side by eminences of* 100 *to* 200 *feet.*
Dumfries.	4·61.	The town lies in a hollow, and on an uneven site. *The site extends about a mile from north to south parallel to the river, rises steeply from the banks at the north end.*

Towns on Distinctly Steep or Hilly Sites Showing a Percentage Slightly Above the Average.

Edinburgh and Leith.	4·03 and 4·11.	These sites are notoriously hilly.
Stirling.	4·19.	
Dundee.	4·09.	
Dysart.	4·10.	It is interesting to compare the mortality figures of Dysart with that of Kirkcaldy, of which it is almost a suburb. The hilly nature of the site is almost similar, but Kirkcaldy lies curved round a cup or bay, and this, I believe, causes its higher figure.

Towns on Slopes Showing a Percentage Below the Average.

Falkirk.	2·68.	*The site is partly a gentle hillside, partly low level ground.*
Eastwood.	3·11.	Near Glasgow, and contains the town of Pollokshaws. *The surface westward declines to* 50 *feet above sea-level, rising to* 167 *feet,* 170 *feet,* 221 *feet, and* 302 *feet.*
Cambusnethan.	2·99.	Contains the towns of Wishaw, Newmains, Coltness, etc. *The tract along the Clyde sinks to less than* 100 *feet above sea-level; the surface thence has a general eastward rise.*
Kilmarnock.	3·80.	*The site slopes gently to the south.*
Dunfermline.	3·93.	*Its site is variously flat and sloping.*
Hamilton.	2·48.	*The town is situated in the midst of a pleasantly diversified ridge, sloping on the whole to the east, north-eastward.*

Paisley.	3·02.	*Part of the site of the burgh is a gentle, hilly ridge. Part is the north side of a similar ridge, and the rest is partly low ground lying between and around these ridges.*
Greenock.	3·12.	*The shore is fringed by a strip of level ground: beyond, the surface is hilly.*
Port-Glasgow.	3·86.	*There is a flat strip along the Clyde from* 13 *to* 20 *feet above sea-level, and from this the ground slopes rapidly up.*

Towns Occupying a Flat Site and with Comparatively Flat Surroundings Showing a Mortality much below the Average.

Dumbarton.	1·80.	*Its site is a low flat plain.*
Kirkintilloch.	1·75.	The conditions here are similar to Dumbarton.
Alloa.	2·45.	*The carse lands around it consist of alluvial flats.*
Peterhead.	2·79.	The town is surrounded by a wide tract of flat country.
Glasgow.	2·98.	*The site, especially towards the east and south, is very flat, as it also is on the north along the side of the river. Nowhere in these districts is it more than a few feet above the level of the spring tides.*
Kinning Park.	1·76.	A suburb of Glasgow.
Govan.	2·08.	A suburb of Glasgow. *Along the Clyde is low and flat, varying in height from* 19 *to* 24 *feet at Govan burgh.*
Rutherglen.	2·14.	A suburb of Glasgow. *The portion of the parish along the Clyde is from* 30 *to* 40 *feet above sea-level.*
New Monkland.	2·36.	This district includes the town of Airdrie. *The dorsal ridge that runs through it from end to end ascends from so broad a base so gently and continuously as nowhere to form any height, which, properly speaking, can even be termed a hill.*
Coatbridge.	2·69.	Similar to New Monkland.
Dalziel.	2·29.	This district includes the town of Motherwell. *Sinking to less than* 100 *feet above sea-level, it forms in the centre, and towards the south-east, a flattish ridge or low plateau.*
Old Kilpatrick.	2·80.	Contains the burghs of Clydebank, Bowling, etc. *Low flat ground along the Clyde.*

From these groupings it will be seen that the towns lying in a cup have by far the highest cancer mortalities, while those on a level site with level surroundings show the lowest percentage. Those on hilly sites are slightly higher than those on sloping sites.

When the situation of a town seems to have so marked an influence upon its cancer mortality, it would be even more valuable if it were possible to discover whether there were certain portions of towns more liable than others. This, however, so far as statistics go, it is impossible to discover. There has been, however, a most interesting piece of work done by Behla on his own town of Luckau in Germany which seems to me to bear very strongly upon this subject, although Behla himself does not specifically mention it. In the course of twenty-two and a half years' practice in this town of Luckau he noticed that while he had never met with a case at all in the Sandoer suburb, in the Kalauer there was hardly a house which had not had several cases in it. In order to show the lie of the ground and the relative positions of the two portions of the town, I have had it specially photographed. The Sandoer portion, in which no case had occurred in the twenty-two years, lies on the

Möbel-Magazin.
Fleischerei – P. Müller.

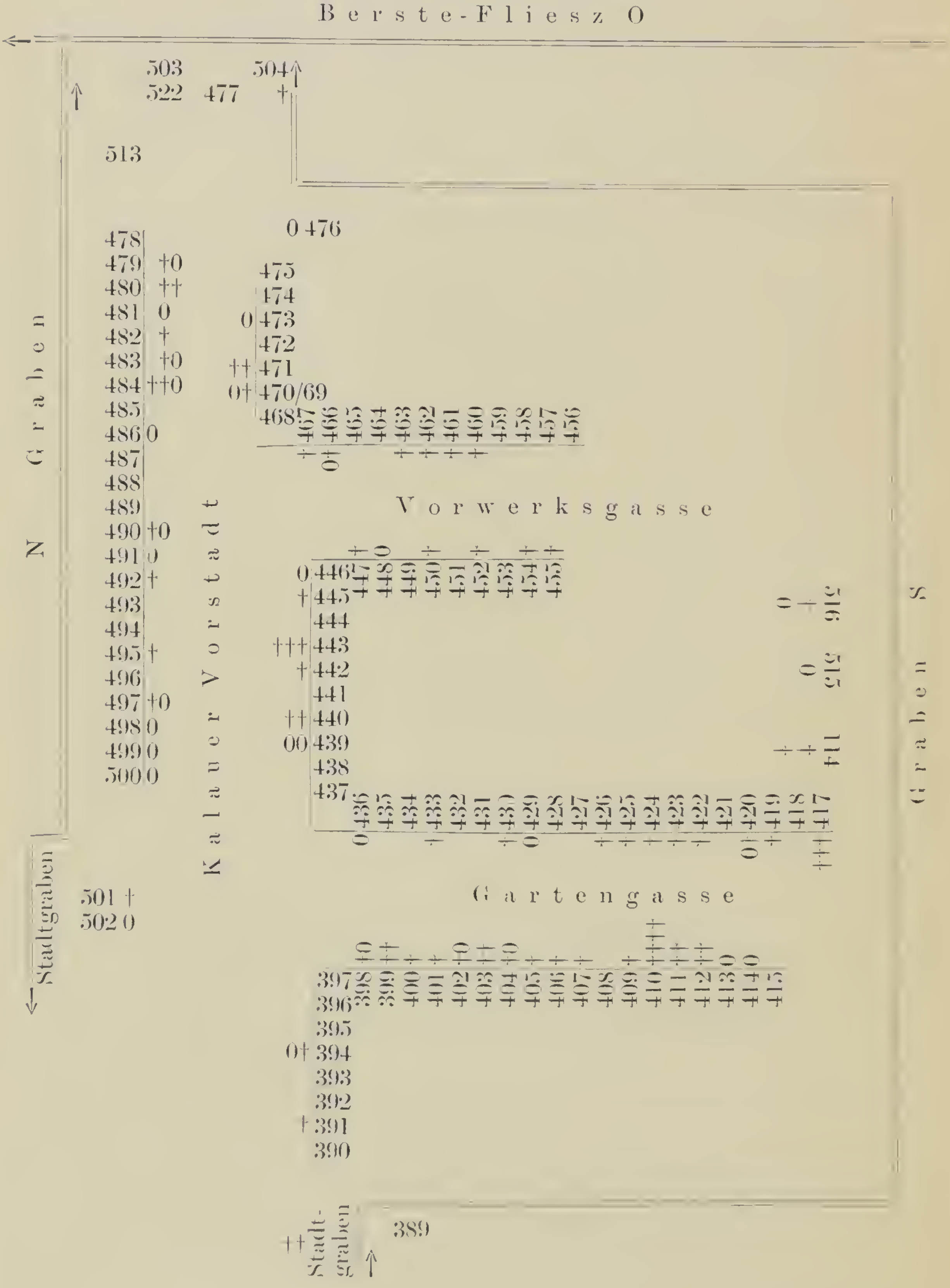
extreme right on the height; the Kalauer lies *in the hollow*. The following is a translation of a portion of Behla's paper:—

I have been practising for twenty-two and a half years in Luckau—since October 1875. It numbers about 5000 inhabitants, including some 500 inmates of the female prison. The plan of the streets is easy to grasp. The town consists of a central portion (Rundtheil) encircled by a moat, and containing two principal thoroughfares, the Langestrasse and the Hauptstrasse, with a few cross streets and back alleys. Joining on to it on the east and west are two long straggling suburbs, the Kalaner Vorstadt and the Sandoer Vorstadt, each of them with about 1000 inhabitants. The Kalauer Vorstadt has to the south of it two more cross streets, the Gartengasse and the Vorwerksgasse. The number of inhabitants has remained stationary to the present day, and in particular the Kalauer Vorstadt has retained the same number of houses.

In the course of my practice it struck me that cancer, *which was never to be met with at all in the Sandoer Vorstadt*, but occurred not infrequently in the town itself, was very common in the Kalauer Vorstadt, a circumstance to which I felt constrained to devote special attention. Reckoning for the whole town, only one death out of every 25 to 30 was found to be due to cancer, whereas the proportion in the Kalauer Vorstadt was an exceedingly striking one. From October 1, 1875, to April 1, 1898, 663 deaths occurred in this part of the town, 73 of these being due to cancer; we have therefore already on an average 1 death from cancer in every 9—a very high proportion in comparison with that of other places; almost as high as that of tuberculosis in our district (1 death from phthisis in every 7 or 8).

Speaking generally, and with local variations, we count, in Prussia, 1 death from cancer in every 50—30; Frankfort a/O, for instance, shows a larger proportion—1 in 23—and here, in the Kalauer Vorstadt of Luckau, we get a percentage which very nearly approaches that of Vignes, in Cormeilles (15 per cent.). Moreover, in this district, an increase in the number of cancer cases is to be noted. Indeed, from January 1, 1897, to April 1, 1898, *i.e.* in $1\frac{1}{4}$ years, 10 people have died there of cancer out of a population of 1000.

Luckau (Kalauer Vorstadt).



For greater ease in studying the matter, I have marked each case of cancer in the accompanying plan according to the house in which it occurred. The numbering of the houses runs from 387 to 516 and I have designated them in the plan with these numbers in their order. The houses in which cases of cancer occurred between October 1875 and April 1898 are distinguished by a cross.

No doubt as to the correctness of the diagnosis—"cancer"—can be admitted. No sections were taken, it is true, and apart from the case of operations for cancer of the breast, the histological structure of the growths could not be more precisely ascertained, but every case was examined by me personally, and the tumours palpated. The course of the disease, its clinical appearance, the usual death, etc., left no doubt as to the correctness of the diagnosis, which was also confirmed by other practising physicians. I also looked through the available records of deaths as far back as 1852. They are in the custody of Herr Oberprediger Schippel, who readily gave me leave to examine them. Of course statements of a very general character abound in them, the cause of death being given as dropsy, jaundice, consumption, etc. Old-fashioned surgeons were fond of these broad diagnoses. The possible causes of death with which they were acquainted were few. But the practitioners of the present day are more precise. In the more recent records a number of cases occur where the cause of death is stated to have been, primarily, cancer. These also I have entered in my plan of the Kalauer Vorstadt, marking the houses where they occurred with an O.

A glance at the plan shows us that by far the greater number of houses have been visited by cancer. Indeed the number should doubtless be larger still, the terms "dropsy," "jaundice," "consumption," etc., in all probability often serving to conceal some malignant disease. The computation is therefore more likely to be too low than too high.

We may note that just in the Gartengasse, and particularly on the west side, cancer has made great inroads; it is a veritable "cancer street." We might indeed, following Gueillot, speak of actual "cancer houses," as the houses No. 410, 417, 413 testify, for in these we find, in the comparatively short space of twenty-two and a half years, 3, and in one case 4, cases of cancer occurring in a single house. This cannot be pure chance. There must be some cause; some particular infective agent must be responsible for this prevalence of cancer in one small district.

In Luckau, therefore, we find that cancer is very prevalent in the hollow, and to further illustrate the relationship of the lie of the ground to malignant disease in the case of an even more restricted district, I annex a plan given in Murphy's *Surgery*, Fig. X., illustrating a cancer district which Mr. Murphy had personally investigated, and on the strength of which he suggests that the condition is infectious. This plan is worthy of most careful study, as the author has indicated the slope of the ground by arrows. If these arrows are followed, they will be found in a most remarkable way almost to point to the houses in which cases have occurred. The first case occurred in a house at the top, but it is a corner house, and it has often been claimed that in corner houses cases are very common; all the others follow exactly the contour lines of the falling gradients.

If, then, the lie of the ground seems to have a mysterious influence on the local incidence of cancer, how can this be explained?

When I first realised that the disease was more prevalent in certain districts than in others, I began to carefully examine the exterior of all the individual houses in which I could discover that cases

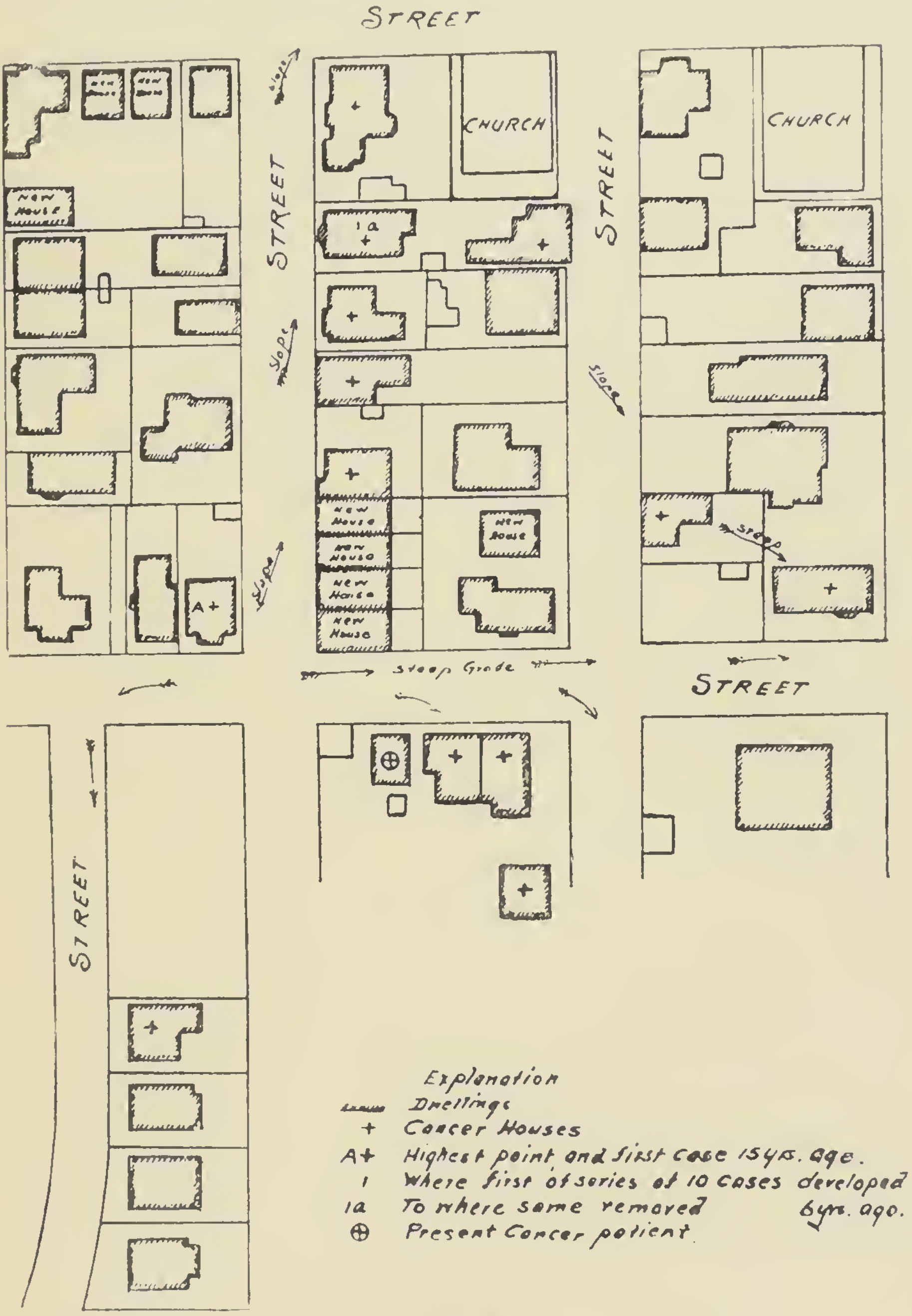


Fig. X.

had occurred in my own neighbourhood. I disregarded cases in which the occupants had been less than three years in the house and also those of men who went out to business all day.

For a long time I could find nothing in common between these houses, which were of all descriptions. from isolated country cottages to large suburban mansions and city flats, until it occurred to me that nearly all of them had appliances on the chimneys, evidently designed to encourage and increase the draught. A further inquiry elicited the fact which one would have expected, viz. that in nearly all of the houses the rooms were smoky.

I venture to make the assertion that almost without exception houses in which cases of cancer have occurred have badly drawing chimneys, or are exposed to smoke from outside chimneys, the tops of which are on a level with the windows of the affected house.

This question of the relation of chimneys and of smoke to cancer has never been previously referred to, but I believe that it furnishes one of the keys to the problem. The products of combustion in a room must either go up the chimney or out into the room. If the chimney is defective the latter result ensues. A proper chimney should carry all these products out into the atmosphere. Wherever cowls or other appliances are placed on the chimney heads it is a proof that the smoke has in that chimney a tendency to come out into the room instead of being drawn up. It must be borne in mind also that fumes may be coming out into a room although no smoke is visible.

Wherever the head of a chimney is below the level of the surrounding roofs or of the surrounding ground, the tendency is for the smoke not to rise. In this way it will often be found that the chimneys on one side of a house will not draw, while those on the other draw excellently. In the same way on a slope, the chimneys of the houses at the top of the slope will usually be found to draw better than those at the bottom. Trees often have the same effect as an adjoining roof or an adjoining slope. The whole question of the relationship of the draught of chimneys is most fully and interestingly dealt with in a quaint but very scientific little book, which is a reprint of an article in the *Encyclopædia Britannica* "On Smoky Chimneys," and the following extract is quite germane to the present inquiry :—

> To illustrate this more plainly, let A B, Fig. XI, represent a part of a high building, near to which is a smaller one, C D; and let the dotted line, E F, represent a current of air flowing with considerable force in the direction of F E. It is plain that it will flow straight forward over the top of the small building; but when it meets with the large object, it will be interrupted in its course and spread itself on every side, as represented by the dotted lines G G, etc., and at last it will flow towards that place through which it can escape with the greatest ease. If the opposing object be

large, and if there be no opening through which it can issue near the ground, then it will ascend to the top of it, and flow off in that direction, carrying the smoke that ascends from the small chimney, C, along with it: but if there is any opening below, either a street or lane, or any other passage that will admit the wind to pass, then will the natural gravity of the air draw the general current downward to flow off through the lower passage; in which case, the smoke which ought to ascend through the chimney, C, meeting with a current of air opposing its passage, will not be at liberty to issue forth, but be forced back again into the room from whence it proceeded, unless some contrivance is fallen upon to prevent it.

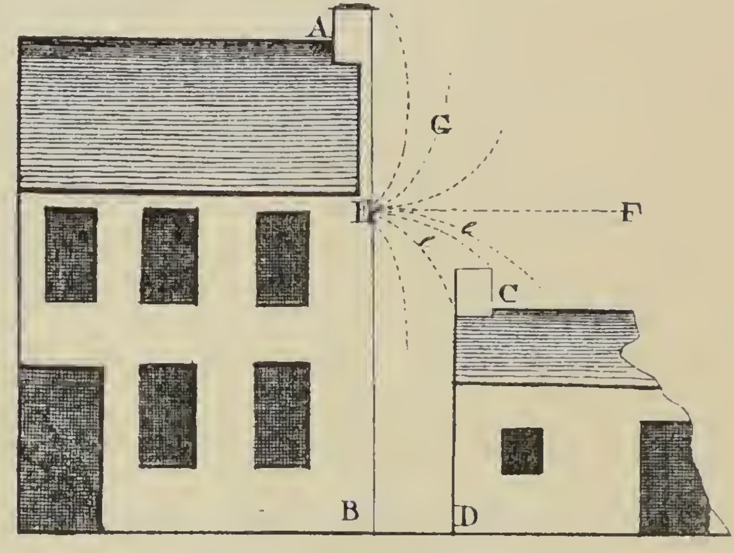


FIG. XI.

Again, let A, Fig. XII., represent a small building at the side of a great rock, B, and the wind coming in the direction C D; when the current of air comes to the point D, being hurried forward with great velocity, it goes a little forward, but soon declines downward, and gradually is inflected more and more inward, as represented by the dotted lines E E, etc.; so that pressing downwards upon the top of the chimney, A, the smoke is beaten back again into the apartments. Thus it is that low houses, when contiguous to high objects, are in danger of being disturbed with smoke.

· It is evident that houses situated near high hills, or thick woods, will be in some measure exposed to the same inconvenience;

but it is likewise plain that if a house be situated upon the slope of a hill, as at F, it will not be in any danger of smoke when the wind blows towards that side of the hill upon which it is situated; for the current of air coming over the house-top in the direction of G H, is immediately changed, by the slope of the hill, to the direction H C, which powerfully draws the smoke upward from the top of the chimney. But it is also evident that a house in this situation will be liable to smoke when the wind blows *from* the hill; for the current of air coming downward to the direction C H will beat downward on the chimney, F, and prevent the smoke from ascending with freedom. But the effect will be much heightened if the doors and windows be chiefly in the lowermost side of the house.

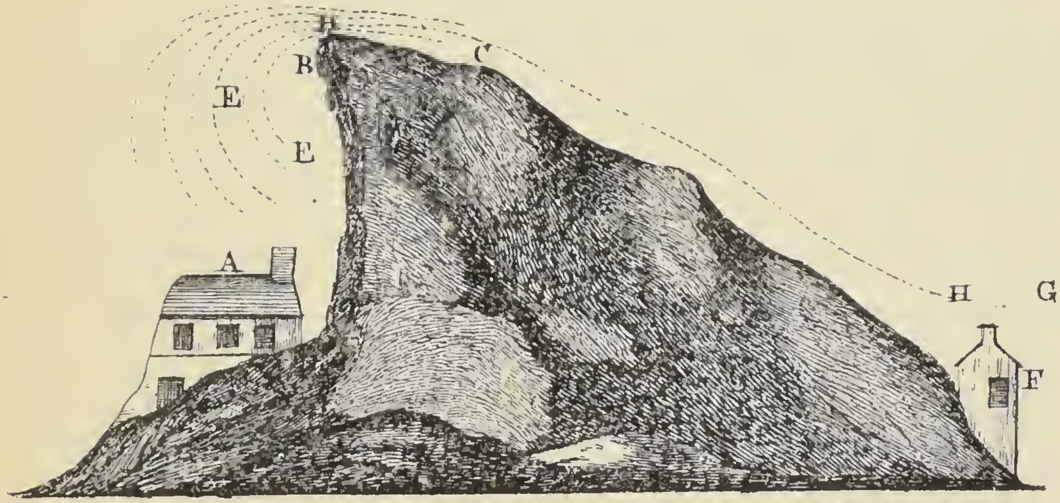


Fig. XII.

Too much may seem to have been made of this point, but there is no gainsaying the fact that in tropical countries where there are no chimneys the disease is almost unknown. In Jamaica, for example, where there are no house-heating chimneys, and where all cooking is done outside, the cancer death-rate is almost inconceivably small, viz. 1·6 per 10,000 living.[1]

In the same way the cancer mortality of the Northern States of America is double that of the Southern States.

In Mexico, according to Jourdanet, it is almost unknown in the hot regions, whereas in the cool regions on the high plateaux it is frequent. My explanation of this would be that in the high plateaux they have to burn fires. In the hot districts they do not.

Roger Williams, in his interesting chapter on the geographical distribution,[2] sums up by saying that the disease seems to increase in frequency with remoteness from the Equator, and asks how the much greater prevalence of malignant tumours in temperate than in hot climates which his world-wide survey reveals can be accounted for. To my mind it is obvious. The further from the Equator the greater necessity for artificial heat, with the concomitant products of combustion.

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[1] This low death-rate was lately disputed by a well-known authority on the ground that it was unreliable, since only a proportion of the deaths were medically certified. I have, however, had the opportunity of discussing it personally with the Registrar-General of Jamaica, who states that exactly 71 per cent. of the deaths in Kingston are medically certified. The deaths from carcinoma in Kingston for 1908 were 9; from sarcoma, 1; from malignant disease not otherwise defined, 8. The total deaths in Kingston for the same period were 1959, so that *cancer accounts for only* 1 *death per* 100 *in Kingston.*

[2] *Natural History of Cancer*, p. 22.

It is a curious fact, too, that in many countries while the white population suffer severely, the aborigines, who live differently and do not warm themselves by artificial heat, are immune.

A striking case in the other direction is that of the American negro. Chisholm's statistics show that before the emancipation the whites were more than twice as liable as the blacks. The planters gave their slaves wide, airy rooms, plenty of simple food, and much outdoor labour. Since the negress has lived in her own house her death-rate from uterine cancer has become 20, as against 15·7 for her white sister. In the same way the North American Indians were exempt from cancer in their primitive savage condition, but with modern civilisation their comparative immunity has now passed away.

Even some of the exceptions to the statement that the disease seems to increase in frequency with remoteness from the Equator seem to me to bear out the accuracy of my suggestion. It has been pointed out, for example, on more occasions than one that the disease is rare in Iceland. Dr. Jefferson, who visited these islands in 1892, informed Dr. Roger Williams that the disease was then very rare. During some months' residence he never saw a case in Iceland. In 1890 there were only two deaths from cancer in the whole of Iceland. In 1900 twenty-two such deaths were notified. I have taken some trouble to inquire into the conditions in Iceland, and find that until lately no coal was used at all. The ordinary grate is still almost non-existent; stoves which burn peat or turf being generally used. Coal, however, is now being imported to a considerable extent.

In the Färöe Islands, again, cancer was quite unknown until lately. Panum saw no case of it during his residence in these islands, nor could he hear of any. Davidson, in his *Geographical Pathology*, as late as 1892 (vol. i. p. 13), says: "Here, then, we have a country from which this terrible scourge of humanity is absent."

Now, in the Färöe Islands we have a most interesting set of conditions. In Lanat's description of the "Feroe Islands," 1810 (the authority on the subject), we are told, regarding the kitchens, that "they have no chimney (p. 382), but on one side a few large stones laid on the floor serve as a fireplace, and some stones or bricks placed behind it prevent the wooden wall from being damaged by the fire. A square hole in the roof admits the light, and at the same time gives vent to the smoke. In rainy weather this hole is covered with a board." "It is very remarkable, as there are no chimneys in such apartments, and though the wooden walls are so near the fireplace, that fires are scarcely ever heard of. This seems to be owing to two causes: the first that the timber used for building is floated and impregnated with salt water. The second is that *nothing is burned here but turf.*"

As to present conditions, I have lately been in correspondence with Mr. Coates, the British Consul, who has kindly given me some details. "Cancer," he writes, "is not now an altogether unusual disease in the Färöe Islands. The Färöese use open hearths and stoves, in which turf is generally used as fuel; *some coal is now, however, being burnt at the larger towns.*" The conditions seem to be similar to those of the cottars in the Lewes, where cancer is also almost unknown, and where the open turf hearth is the general rule.

Nowadays we are so used to the combustion of coal that we think nothing of its smoke and sooty deposits. This was not always the case, however.

That the fuel was received at first with disfavour appears from the fact that in the reign of Edward I. the nobility and gentry made a complaint to the king objecting to its use, on the ground of its being a public nuisance. By the middle of the seventeenth century the use of coal was becoming more general in London, chiefly owing to the scarcity of wood; and its effects upon the atmosphere of the town will be inferred from a proclamation issued in the reign of Elizabeth, prohibiting its use during the sitting of Parliament, for fear of injuring the health of the knights of the shire. About 1649 the citizens again petitioned Parliament against the use of this fuel on account of the stench; and about the beginning of that century "the nice dames of London would not come into any house or roome when sea-coales were burned, nor willingly eat of meat that was either sod or roasted with sea-coale fire" (*Stow's Annals*).

An open hearth with a hole in the roof, is totally different from the ordinary coal grate with an open fire, and in some cases fifty or one hundred feet of chimney between it and the open air. Custom has reconciled us to what our ancestors took serious exception, but I am convinced that we have had to pay the price in an increased susceptibility to malignant disease from the products of coal combustion by means of the grate and chimney. Among the products of that combustion are sulphurous acid, sulphur dioxide, and sulphur trioxide. These gases are heavier than air, and are very apt to come out into the air of the room under the chimney conditions which I have mentioned. Although the smoke may seem to be drawn up, it does not follow that all the sulphur oxides follow.

In addition, we have the accumulation of soot and coal tar in the chimney. In many rooms with windows and doors closed the only possible source of ventilation is down this filthy, soot-lined tube. It does not require much argument to prove that if there be not a constant current of air *up* a chimney, whether a fire be beneath it or not, the air of the room must be contaminated by soot and sulpho-acids.

CHAPTER IV

A SUGGESTED EXPLANATION

If the hypothesis put forward in the previous chapters be correct, and if a fungoid parasite akin to the myxomycetes be the cause of the disease, how can sulphurous acid or the sulpho-acids affect the growth of such an organism?

To begin with, all fungi can *directly use* sulphurous acid and hydrosulphurous acid (H_2SO_3, H_2SO_2), if present in sufficient dilution to be non-poisonous (Pfeffer, *Plant Physiology*, vol. i. p. 429).

patients alkaline

Again, De Bary points out that the lower fungi, unlike bacteria, grow best in an acid solution, and that if the solution be made strongly alkaline, growth will cease.

It has lately been shown too that the lower fungi, such as the yeasts, flourish best when sulphates are present as part of their inorganic nourishment. The sulphate can be effectively replaced by thiosulphate or sulphur, but not by thiocarbamide, potassium sulphocyanide or sulphonal (Matthew's *Alcoholic Fermentation*, p. 277).

That manures dissolved in sulphuric acid foster the growth of *Plasmodiophora brassicæ* to such an extent that the Board of Agriculture thinks it advisable to circularise farmers on the point has, however, already been pointed out. Sulphuric acid itself in the soil does not seem to be alone responsible, since turnips have been grown experimentally in soil impregnated with it without finger-and-toe resulting. What does, on the other hand, frequently cause the disease is bones dissolved in sulphuric acid and used, as they frequently are, as a manure. The change which the acid effects on bones over which it is poured is shown by the following analyses:—

Raw Bones

	Bone Meal.	Bone-Char (dry) after treating Bones in Closed Retorts.
Moisture . . .	10·43	...
Organic matter[1] . .	32·30	10·51 (carbon)
Phosphates of lime and other bases . . .	48·40	80·21
Carbonate of lime, magnesia, etc. . . .	7·20	8·47
Insoluble silicious matter, ferric oxide, and alkalies .	1·67	0·81
	100·00	100·00

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[1] Containing 3·71 of nitrogen = 4·51 of ammonia.

BONES DISSOLVED IN H_2SO_4

Moisture	10·10
Organic matter and water of combination[1]	29·34
Monocalcic phosphate of lime	11·23
(Equal to tricalcic phosphate rendered soluble	17·58)
Phosphate soluble in ammonium citrate	14·02
Insoluble phosphate of lime	1·88
Calcium sulphate, etc.	30·23
Sand and impurities	3·20
	100·00

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These analyses show that the effect of the H_2SO_4 is to largely replace the phosphates and carbonate of lime by calcium sulphate.

Now blocks of gypsum, which is calcium sulphate combined with $_2(H_2O)$, are the regular method for the cultivation of the spores of saccharomycetes in laboratory practice, as a richer spore formation is got on gypsum than on other substrata (Klöcker, *Fermentation Organisms*, p. 64). This result is due not only to the effect of the calcium sulphate on the yeast, but also to the fact that it prevents the growth of bacteria (Klöcker, p. 65).

Hansen, who is the greatest authority on yeasts, brought out a remarkable fact in connection with spore formation in relation to calcium sulphate, namely, that the spore itself can occur as a spore mother-cell. This happens when the spore, after being a short time in a culture liquid containing sugar, has swelled up and is then transferred to an aqueous solution of calcium sulphate. *No buds are then produced, and instead spores are formed in the interior of the swollen spore* (Klöcker, p. 205). This fact is of great importance in relation to cancer cytology.

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[1] Containing nitrogen, 2·62=3·18 ammonia.

From the behaviour of the yeast plant we can also infer that it is only when such lower forms of fungi are deprived of *free oxygen* that they become as it were malignant in their effects upon their hosts or on their surroundings; for is not Pasteur's beautiful and rational theory of fermentation that it is a vital phenomenon caused by the living yeast-cell out of contact with *free* oxygen attacking and breaking down the maltose molecules of the wort to satisfy its own requirements? Pasteur has also shown that cells of others of the lower fungi morphologically similar to the yeast-cell, when deprived of *free* oxygen by being placed in an atmosphere of CO_2, produce similar results. When yeast is steeped in beer wort it first assimilates the free oxygen and then attacks the sugar.

On the assumption, then, that cancer is due to an organism of a fungoid nature, there is little [illegible] cells suffer but [illegible] proliferate -

This is [illegible] (theory) -

doubt but that it will act in a similar way in the tissues. If it cannot get free oxygen, it will attack the cells. In the presence of free oxygen it would be harmless, in the absence of free oxygen malignant.

This question of oxygen is an all-important one in relation to sulphur dioxide, which is a constant product of coal combustion.

In my view the damage caused by SO_2 and sulphurous acid is still greater in absorbing oxygen from the tissues, and so rendering them liable to the attacks of the minute fungi, which grow best in any medium *not too fully oxidised.* The absence of chlorophyll makes these organisms unable to decompose carbonic anhydride, and they must depend upon organic compounds already formed. Almost any soluble carbon compound *not too poisonous or too fully oxidised* will serve, and similarly with most nitrogen compounds, even urea.

It has been found that *Plasmodiophora brassicæ* is unaffected when the oxygen present is only $\frac{1}{300}$th of that in the atmosphere.

SO_2 (*i.e.* sulphurous anhydride, sulphur dioxide, or, as it is often called, sulphurous acid) is a powerful deoxidising agent. Indeed, if the gas be dissolved in water it rapidly absorbs oxygen and is converted into H_2SO_4.

Sulphur dioxide as a gas is very injurious to animal life, and is an acute blood poison. Ogata (*Archiv. f. Hygiene*, 1884, p. 223) found that 0·04 per cent. of SO_2 in the air causes difficulty of breathing after a few hours. He could not take a single full breath in air containing 0·05 per cent.

From air containing as little as $\frac{1}{5000}$th of its volume of SO_2, this gas is absorbed by the leaves of trees. These retain it chiefly, a smaller portion penetrating into the wood, either as such or after oxidation to sulphuric acid.

Hasenclever, in his monograph on the damaging effects of acid gases on vegetation (Berlin, 1879), deals fully with the question, and gives several illustrations showing the effects of sulphurous acid gas. He shows also that the evil effects are worst in damp weather. In dry districts SO_2 has little or no effect, while in moist valleys it causes spots on the leaves in a few hours, and appreciable quantities of sulphuric acid can be removed from the leaves and stems of plants.

Morren (*Chem. Trades Jour.*, ii. p. 188) says "when sulphurous acid is present in a proportion of 1-80,000 the leaves of fruit trees are visibly affected in three to five hours, and *this effect seems to spread after direct action of the gases ceases.*

Adult leaves are usually more sensitive than young leaves. Sulphurous acid dissolved in water is almost without effect in the upper leaf surface, while in the lower surface each little drop causes the formation of a spot visible on the surface. This solution is not quickly changed into sulphuric acid, whose direct effect is quite different from that of sulphurous acid, since the latter, whether as a solution or in a gaseous state, is as potent by night as by day."

These effects on vegetable tissues are almost certainly due to the deoxidising effect of SO_2. Its effects on human tissues must be similar, although it may be slower in action. People who live in an atmosphere constantly charged with it must not only inhale it, but, as in the case of trees, it must penetrate into their pores and cause a deficiency of oxygen in their blood-stream and tissues. The latest teaching of physiology is that the cells of the tissues use the oxygen of the blood directly, that the oxygen enters the cell by diffusion, and further, that the amount of oxygen taken up by the cell is greater in youth than in old age. The cells of elderly people have, therefore, naturally a less supply of oxygen, and are accordingly more liable to cancer, if cancer be due to a fungoid parasite.

A deficiency of free oxygen would also be greatest where cancer is most prone to occur, viz. on mucous surfaces, where the supply of oxygen in the blood will be least. The very fact that the pulse-rate is increased in malignant conditions shows that the tissues are calling for more oxygenated blood.

It is an undoubted fact, which has been pointed out more than once, that those predisposed to cancer have small lungs and a small pulmonary artery. Beneke, Cattin and Roger Williams agree on this point.

It was also shown as far back as 1843, that in cancer patients the red blood corpuscles were greatly reduced in number, and this has since been abundantly proved.

Other observers have pointed out that in the blood of cancer patients hæmoglobin is very greatly reduced. 1000 grammes of normal blood contain about 125 grammes of hæmoglobin, whereas in cancer cases the amount often does not exceed 25 grammes. The difference between cancerous and non-cancerous blood in this respect is so marked and constant that Laker maintains it may be relied on for the purpose of differential diagnosis. Marked diminution of hæmoglobin may be detected even before the patient's health breaks down. This deficiency of hæmoglobin must result in an enormous deficiency of oxygen in the tissues since hæmoglobin plays the part of a middleman between the air and the tissues, taking oxygen from the one and handing it to the other.

At the temperature of the body the blood can hold in solution less than 1 per cent. of oxygen while the amount of oxygen actually present is about 20 per cent., so that by far the greater quantity of the gas is not in solution, but in loose chemical union with hæmoglobin.

?

sphere air composed

- Nitrogen

- Oxygen.

CHAPTER V

IS CANCER CURABLE?

If it is probable that the conditions affecting the trades showing the highest cancer mortality figures might furnish a clue to the etiology, it seems equally probable that some light might be thrown upon the prevention, and, conceivably, even the cure, of malignant disease by an inquiry into the conditions affecting those occupations in which it occurs with least frequency.

From the Registrar-General's latest returns it will be seen that these trades are *tanners*, which show the lowest comparative mortality figure, 33; *papermakers*, comparative mortality figure 39; and both *copper-workers* and *copper miners*, which also show a mortality figure of 39, although they work with copper under totally different conditions, a fact which is rather striking, and goes to prove that there is something in the metal itself which is inimical to cancer. The salts of copper, it should be noted, are very powerful fungicides, and sulphate of copper is a constant ingredient in all mixtures used for fungoid

[illegible]

diseases in plants, such as the well-known Bordeaux mixture (Bouillie Bordelaise) and Burgundy mixture, used originally for spraying vines attacked by phylloxera.

The other two trades, viz. tanners and papermakers, seem at first sight to have little in common. It has been said already, however, that the tanner, unlike the furrier, works largely with lime. In order to remove the hair the hides have to be steeped in lime pits, and enormous quantities of lime are used for this purpose. The papermaker, again, prepares his fibre, from which the paper is made, by bleaching it with strong chloride of lime. A fair-sized mill will use from twenty to thirty tons of chloride of lime every week, and the strong smell of chloride of lime is continually felt all over every paper mill and its surroundings.

[illegible] is [illegible] when [illegible] ferrous [illegible] the region [illegible] cancer

Now, to revert for a moment to the question of *Plasmodiophora brassicæ*, it is a commonplace among farmers, and is mentioned in every agricultural treatise, that the only known method of eradicating this organism from land is by the use of lime. Further, plants suffering from the disease are never found on calcareous soils, nor on soils which are heavily charged with lime (*Encyclopædia of Agriculture*, vol. ii. p. 104).

Dr. Marshall Ward, than whom there is no higher authority, in his work on *Disease in Plants*, says: "Finger-and-toe, due to Plasmodiophora, has been successfully dealt with by the application of lime, but we do not know whether the effect is owing to indirect action on the soil, to direct action on the plasmodia, or to the increased production of root hairs caused by the liming."

Again, the Board of Agriculture official leaflet, No. 77, says: "Finger-and-toe is practically unknown on soils naturally containing a high percentage of lime. The artificial application of burned lime has long been practised as a preventive, and this substance is still the most effective agent that is known. Other forms of lime are more or less effective, though none is so powerful as common burned limestone. Chalk has also a preventive influence, though its effects are weaker than those of burned lime, and from two to three times as much should be applied."

If the theory which I have tried to enunciate in the preceding pages be based on a fallacy, this matter of lime is of no importance. If, on the other hand, there be anything in the opinions of those who believe that cancer is due to an organism akin to the myxomycetes, the question of the relation of calcium to the prevention and even the cure of cancer may be of supreme importance.

In the *Lancet* for October 12, 1867, there will be found a rather interesting letter by Dr. Peter Hood, of Portman Square, on the effect of oyster shells on a woman eighty years of age, who, he says, was cured of an enormous carcinoma by their use; and also on a man who had a tumour in his cheek as large as a small orange, and was cured by the same means. The shells were baked in a slow oven and the small white part picked out and powdered finely, as much as would lie on a shilling being taken once or twice a day in warm water or tea.

If we can rely on these cases—and there seems no reason why we should not, when the letter is carefully read, it is obviously the lime in the oyster shells which was the curative agent.

As to violet leaves, it seems undoubted that one or two cures have been effected by their use.[1] So generally is this believed, that the wholesale chemists regularly prepare and sell refined infusions of these leaves, which are used daily. That these infusions have no effect is hardly to be wondered at, since in the cases of supposed cure, poultices or direct infusions of the leaves themselves have always been used.

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[1] *Viola Odorata.*—The flowers, leaves and entire plant of the sweet-scented violet have an ancient reputation in the treatment of cancer when taken internally and applied externally. The leaves of the Princess of Wales variety are said to give the best results in doses of 4 drams of a 1 in 1 liquor.

The wild pansy (*Viola tricolor*) is believed to have similar properties of checking the discharge and relieving the pain of malignant growths (Whitla's *Materia Medica*).

Now, if there be any virtue in violet leaves, we may fairly claim it again for calcium, from the amount which leaves contain. They are rich in calcium, and, as Pfeffer points out (*Plant Physiology*, vol. i. p. 585), "in those organs which are not used for storage the accumulated calcium remains for the most part permanently deposited. This is the case, for example, in foliage leaves, in which the absolute amount of calcium continually increases until the death of the leaf."

Lime, as the word is generally used, is monoxide of calcium, CaO, and is made by heating limestone or marble to full redness, when carbonic acid is expelled and lime left. CaO is then known as quicklime, to distinguish it from slaked lime or hydrate of lime CaO, H_2O.

Limestone itself contains a greater proportion of oxygen than lime, and is, like chalk and marble, nearly pure carbonate of lime, $CaCO_3$. It has been already pointed out that finger-and-toe is unknown on limestone and chalk soils, and Havilland states (*Geographical Distribution of Disease in Great Britain*) that cancer is also rare on these soils.

Calcium carbonate itself, $CaCO_3$, is insoluble and cannot gain admission to the tissues of animals or plants. The water in the soil, however, contains CO_2, and this, uniting with the particles of limestone, forms a soluble bicarbonate, $CaC_3O_6H_2$, which is readily absorbed by the tissues, and in the case of plants has a strange and powerful effect. Schimper, in his *Plant Geography*, page 94, deals fully with this subject, and gives some curious instances of calciphilous and calciphobous plants, while Hugh Miller emphasised long ago the mysterious effect of lime in destroying the reptiles, fish, and insects of a thickly-inhabited lake or stream, without injuring a single flag or bulrush among the millions that line its edge (*Old Red Sandstone*, p. 243).

If, then, the existence in the soil of the soluble bicarbonate of lime has unquestionably a deterrent effect upon Plasmodiophora which causes finger-and-toe, and if cancer be due to a morphologically similar organism, this surely accounts for the fact that workers with lime are largely immune.

Indeed, does it not indicate that lime in combination with water and CO_2 would be a valuable therapeutic agent?

The salts of lime are present in very large amount in the tissues of animals, and considerable interest attaches to their absorption, excretion and general action. They form the great mass of inorganic constituents of the bones and teeth of the vertebrates and of the shells of the invertebrates. It has also been shown in recent years that they are present to a considerable amount in the soft tissues. Like other alkaline earths, however, calcium differs from the alkalies in possessing few soluble salts. Even the soluble salts penetrate with difficulty into the various tissues. They precipitate colloids such as the proteins in much more dilute solutions than the alkalies, and the precipitate is not redissolved by dilution with water.

The soluble lime salts are absorbed with great difficulty from the stomach and intestine. The great proportion of lime taken in the food unquestionably leaves the body entirely unabsorbed, while a small quantity is taken up from the alimentary canal whether administered in a soluble or insoluble form. This small quantity circulates in the blood probably in combination with proteins, and is slowly excreted unless there is a deficiency in the supply of lime, when it may be utilised by the tissues.

When larger quantities are thrown into the blood by intravenous or hypodermic injection the calcium of the blood remains abnormally high for some time, but all the calcium thus injected is not in the circulation throughout its stay in the body, some of it is temporarily deposited in some unknown organ, and is gradually withdrawn and excreted after the first excess is eliminated. Soluble calcium salts injected directly into the blood-vessels have an action resembling that of digitalis. They also markedly contract the vessels. Large quantities injected intravenously contract the pupil to pin-point size, apparently from action on the sphincter muscle, as atropine has little effect. These effects are absent when the salts are taken up from the intestine, partly due to slow absorption, partly to the formation of albuminous compounds.[1]

The action of calcium upon the fluidity of the blood is of course well known, and some of its other effects are curious, as, for example, the action of calcium lactate upon chilblains and the influence of lime water upon warts. It was lately stated in the *British Medical Journal* that a patient who suffered from warts, which no treatment would alleviate, was cured within a few days by drinking lime water.

If, then, lime has such an effect upon warts, it is at least conceivable that it might have an effect upon malignant tumours?

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[1] Cushny, *Pharmacology*, 5th ed., 1910.

The connection between calcium and certain enzymes, thrombase, and particularly pectase, is very striking (see Reynolds Green's *Fermentation*, pp. 272 and 291). The action of pectase indeed depends entirely upon the reaction of the medium and the amount of calcium salt which it contains.

In whatever way it may act, I am convinced that calcium is, in inoperable cases or even after operation to prevent recurrence, worthy of a long and systematic trial, administered internally or by hypodermic injections.

It should also be borne in mind that the parathyroid secretion in some way controls the calcium exchange of the body,[1] that the thyroid gland is said to be invariably atrophied in cancer cases,[2] and that the administration of thyroid extract has been followed by an amelioration of the condition.[3]

Finally, should cancer be due to a parasite akin to the myxomycetes or the mycetozoa, there might well be an even more certain method of treating it, since a fungoid organism in order to flourish must have its optimum temperature. A great deal of work has been done in this direction, which shows

[1] *Osler's System*, vii. p. 808.

[2] Bell, *N. Y. Med. Record*, 1907, p. 260.

[3] Stiles, *Ency. Medica*, vii. pp. 337, 338.

that the germination temperature of parasitic fungi approximates naturally the temperature of the body of the host. Thus, those species which are in the habit of germinating in the digestive canal of warm-blooded animals have an optimum corresponding, as might be expected, with the temperature of the body of the animal. The normal temperature of different animals varies,[1] which may account for the comparative immunity of certain animals.

Although all such organisms have an optimum temperature, they have also a minimum and maximum. As a rule the minimum is very low, in some cases extreme cold having been borne without the power of germination having been in the least affected.[2] On the other hand, the maximum temperature does not anything like so greatly exceed the optimum, and the very great majority of minute fungi are destroyed by a temperature of about 50° C. It has been found, for example, that the Ray Fungus, which is the cause of actinomycosis, has an optimum temperature of 32° to 37°, that growth is very slow at 38° C., and is arrested altogether at about 50°. A temperature of 70° for ten minutes has killed it altogether.

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[1] The normal temperature of the horse is 100·2, of the cow 101·4, and of the sheep 104.

[2] See p. 9.

Now, in view of these facts, if cancer is due to a kindred organism, that organism should be destroyed by a temperature of 50° C. or 130° F. It may be said that a temperature in excess of this failed years ago when the actual cautery was applied, but this was a fierce dry heat, and much too limited in its application. Hot water or poultices are entirely different.

My anxiety to test the remedial effect of heat in this way was kindly met by the late Dr. Joseph Bell, who applied water at this temperature to a case of advanced epithelioma of the glans penis, with the result that the primary sore entirely healed up, although the secondary growths, which made the case inoperable, were unaffected. Such a result seems to be fraught with great possibilities.

In any case, I am convinced that a long and systematic trial of the effects of calcium and of heat upon malignant disease would not be without its results.

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